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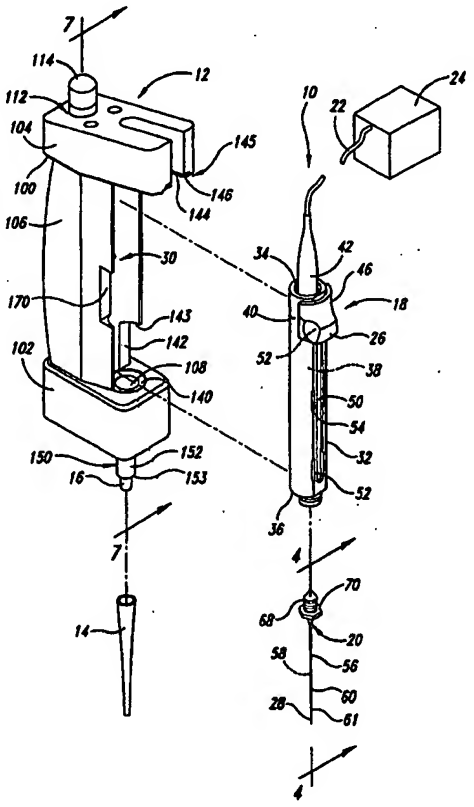
(57) Abstract

The sensor assembly (10) is releasably attached to the sample drawing device (12), such as a pipette and has a sensor carrier (18) with a coupling member (26) attached to a wave–guide cable (22, 208) connected to the electromagnetic radiation source (204). The sensor (20) has a connecting member (68) connectable to the coupling member and a probe (56) projecting from the connecting member. A probe cover (32) is attached to the coupling member and positionable to selectively expose or protectively contain the probe. The sensor (20) is removably received in a protective storage housing when the sensor is removed from the sensor carrier. The sample drawing device includes a drawing mechanism (112) for drawing a selected sample into a sample container (14) and an ejector (150) for ejection of the sample container (14). The sample drawing device is connected to a pneumatic tube (302) that communicates with the sample container, thereby oscillating the sample within the sample container relative to the sensor.



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PIPETTE AND CARRIER ASSEMBLY FOR A SENSOR

TECHNICAL FIELD

The present invention is generally directed toward analytical detection systems for testing a selected sample, and more specifically, toward a wave-guide based chemical-analytical detection system using a sample drawing device and a wave-guide sensor assembly for selectively providing and testing the sample by electromagnetic radiation propagation to and from the selected sample.

BACKGROUND OF THE INVENTION

Chemical-based analytical detection systems are widely used, particularly in the biochemistry and pharmaceutical industries to detect the presence and/or amounts of selected chemicals, compositions, antibodies, hormones, DNA, analytes, or other reagents within a selected sample. Conventional analytical detection systems that use optical sensing systems include systems using evanescent wave-guide sensors, such as is discussed in U.S. Patent No. 5,105,305. Evanescent wave-guide sensors may utilize various physical phenomenon such as surface plasmon resonance (SPR), interferometry, Fabry-Pe'rot resonance, and fluorescence. The sensors may be based on the sample's light emission (*e.g.*, luminescence, fluorescence, phosphorescence, Raman Spectroscopy, or light scattering on surface-enhanced Raman spectroscopy, including surface-enhanced resonance Raman spectroscopy (*see, e.g.*, U.S. Patent No. 4,781,458), and on evanescent wave surface-enhanced Raman spectroscopy (*see, e.g.*, Keller, R., *Applied Spectroscopy 51, No. 4:* 495-503, 1997). For a comprehensive review of evanescent wave-guide sensors see *Dakin & Culshaw, Optical Fiber Sensors: Principles and Components*, vol. 1, chpt. 6 and 9 (1988*) and Culshaw & Dakin, Optical Fiber Sensors: Systems and Applications*, vol. 2, chpt. 16 (1989). Additionally, evanescent wave-guide sensors may be based on measurement of Brewster angle or detection of polarization state by, for example, ellipsometry, frustrated total reflection mode coupling, ring-resonator mode coupling, and evanescent wave spectroscopy.

Another conventional analytical detection system disclosed in U.S. Patent No. 5,416,879 analyzes light absorbed by a fluid drawn into a liquid-core fiber-optic wave guide, wherein the fluid is drawn into and expelled from the wave-guide by means of a fiber-optic plunger. Still another analytical detection system disclosed in U.S. Patent No. 5,253,037 utilizes light leaking through a discontinuous metal layer on an optical fiber.

Other highly sophisticated and accurate optical sensing systems include surface plasmon resonance (SPR) sensors and related detection equipment that are constructed based upon the Kretschmann configuration. In the Kretschmann configuration, a thin layer of highly reflective metal (such as gold or silver) is deposited on the base of a prism or semicylindrical lens, the metal surface is coated with a selected chemical treatment, and a sample, such as a liquid or a gas, is carefully brought into contact with the coated metal surface.

An SPR reflection spectra of the sample is measured by coupling transverse magnetic polarized, monochromatic light into the prism or lens and measuring the reflected light intensity as a function of either the angle of incidence, or the wavelength of incidence, as effected by surface plasmon waves at the boundary between the metal layer and the chemical sample. These optical sensing systems, in conjunction with appropriate chemical sensing layers, have led to the development of a variety of other SPR-based chemical sensors, including immunoassay sensors (*e.g.*, Liedberg et al., *Sensors and Actuators 4*:299-304, 1983; Daniels et al., *Sensors and Actuators 15*:11-7, 1988; Jorgenson et al., *IEEE/Engineering Medicine and Biology Society, Proceedings 12*:440-442, 1990), gas sensors (Liedberg et al., *supra*; Gent et al., *Applied Optics 29*:2843-2849, 1990), and liquid sensors (*e.g.*, Matsubara et al., *Applied Optics 27*:1160-1163, 1988).

While these SPR-based optical sensing systems are highly accurate, reliable, and sophisticated, the systems are typically large and best suited for simultaneous multi-analyte detection in centrally located sensing applications in the area of the large equipment. Such SPR-based optical sensing systems are not particularly well-suited for remote sensing, so chemical samples drawn by a pipette or the like must be brought to the sensing system to conduct the desired sample analysis. The instrument

disclosed in U.S. Patent No. 5,313,264 is an example of such a SPR-based optical sensing system.

A significant development in analytical detection systems, as disclosed in U.S. Patent No. 5,359,861 (Jorgenson et al., October 25, 1994), provided a fiber optic SPR-based chemical sensor that is connected to an electromagnetic radiation source and a detection device. U.S. Patent No. 5,359,861 is hereby incorporated in its entirety by reference thereto. The fiber optic SPR sensor of Jorgenson et al. includes an optical fiber coupled at one end to the electromagnetic radiation source and the detection device, and the optical fiber's opposite end has a sensing area wherein a section of the optical fiber's core wave guide is exposed by removing a portion of buffer and cladding from the core wave guide. An SPR supporting metal layer is symmetrically deposited around the exposed core wave guide to provide a symmetric sensing area of the SPR sensor. These fiber optic SPR sensors are dipped or otherwise brought into contact with a selected chemical sample.

The electromagnetic radiation source provides multiple wavelength radiation through the fiber optic to the sensing area. The detection device monitors the radiation exiting the optical fiber wave guide, thereby allowing for easy, quick, and highly accurate testing. The fiber optic SPR sensors also permit an inexpensive testing system that allows for remote sensing of samples.

These fiber optic SPR sensors detect the presence or absence of the chemical sample by moving the exposed core wave guide and SPR supporting metal layer into contact with the selected sample. The exposed core wave guide and metal layer are fragile and can be damaged or contaminated if the fiber optic sensor inadvertently impacts rigid structures or contacts a surface having a chemistry different than the sample to be tested. Accordingly, a user must use caution during a sampling procedure with these fiber optic SPR sensors to ensure accurate results and to avoid damaging the sensors.

Other fiber optic-based analytical detection systems are known which do not use the SPR detection technique to detect the presence of a selected component or chemical. As an example, a reservoir fiber optic chemical sensor (FOCS), as is disclosed in U.S. Patent No. 4,892,383, provides a reservoir sensor with a semi-permeable

membrane through which a selected chemical species passes to interact with a selected reagent to analyze the chemical species.

Another example includes fiber-optic phosphorous-based sensors which are used to detect phosphorescent components of a selected sample or fluorescent tags applied to particular components of the sample. The degree of change in light into and out of the fiber optic sensor is monitored in order to detect the presences of the reagent for which the sample is being tested. The fiber-optic sensors are dipped into the selected sample. Accordingly, use of the fiber-optic sensor requires the selected sample be provided in a sample container adapted to receive the fiber-optic sensor.

Pipettes and other conventional sampling devices, such as the "Pipetman" model manufactured by Gilson, are used to draw a controlled volume of the sample into a disposable pipette tip, so the sample can be transferred to a selected container or assembly for testing. After the sample has been transferred, the pipette tip is typically disposed of and replaced with a clean pipette tip into which another sample can be drawn. This process of drawing the sample into a pipette tip and transferring the sample to the selected container assembly for testing is a labor-intensive process, particularly when done repeatedly throughout a testing procedure.

Moreover, the prior art pipettes and other conventional sampling devices are typically used only for sample handling (*i.e.*, drawing sample and/or reagents into the pipette tip for subsequent dispensing). The prior art pipettes are not typically used as reaction chambers or flow cells for use with fiber optic-based analytical detection systems. In these systems, flow cells are generally required to ensure that the concentration of analyte in the proximity of the sensing surface is equal to the bulk analyte concentration at all times. In non-flow or static sample environments, the binding of analyte at the sensing surface can cause an analyte concentration gradient across the sample that impedes mass transfer. An analyte concentration gradient may provide less reliable chemical kinetic information.

While conventional wave-guide based sensors and sampling devices are known, there is still a need for wave-guide based analytical detection systems and sampling methods that are inexpensive, easy and fast to use, that provide simplified, consistent and accurate testing with a high degree of repeatability, and that avoid the

drawbacks of the prior art. There is also a need for an improved wave-guide based sensor of an analytical detection system that is protected from damage or contamination during use of the system. There is further a need for a sample drawing device that is usable in conjunction with such an improved wave-guide based sensor to facilitate efficient, inexpensive, and highly accurate testing of the selected samples. There is still another need for an improved analytical detection system that counteracts sample concentration gradients which tend to impede mass transfer to a wave-guide based sensor.

SUMMARY OF THE INVENTION

The present invention provides a sensor assembly and sample moving mechanism, such as a sample drawing device, that overcome the drawbacks experienced by the prior art and provides further related advantages. In one exemplary embodiment of this invention, the sensor assembly is a wave-guide sensor assembly usable with an electromagnetic radiation source and a wave guide cable has a wave-guide-sensor carrier connectable to the wave guide cable and adapted to removably receive a wave-guide sensor. The wave-guide-sensor carrier is releasably received by a sample drawing device, such as a pipette, which is adapted to allow a selected sample to be tested by the wave-guide sensor when attached to the wave-guide-sensor carrier.

In one embodiment, the wave-guide-sensor carrier includes a wave-guide-coupling member attached to the wave guide cable and a sensor-probe cover attached to the wave-guide-coupling member. The wave-guide sensor is releasably attached to the wave-guide-coupling member. The wave-guide sensor includes a connecting member that attaches to the wave-guide-coupling member, and a sensor probe extends through the connecting member and terminates at a first sensing area spaced apart from the connecting member. The wave-guide-coupling member aligns and optically couples the sensor probe with the wave guide cable for propagating the electromagnetic radiation from the wave guide cable through the sensor probe to the sensing area.

The wave-guide-sensor carrier has a probe cover attached to the wave-guide-coupling member. The wave-guide-coupling member is movable relative to the

probe cover to selectively cover and uncover the sensor probe. The wave-guide-coupling member and sensor probe of the preferred embodiment are movable between a sensor-retracted position with the probe's sensing area contained within the probe cover, and a sensor-extended position with the probe's sensing area being exposed and in a position ready for engaging a selected sample.

The wave-guide sensor assembly includes a protective storage housing that is removably attachable to the wave-guide sensor for storage of the sensor when it is not attached to the wave-guide-coupling member. The storage housing of the preferred embodiment contains the wave-guide sensor therein and protects it from being damaged or contaminated.

In one embodiment, the sample drawing device includes a sensor-carrier-receiving portion that receives the wave-guide sensor assembly when the assembly is in an installed position. The sample drawing device has a locking mechanism that releasably engages to the wave-guide-sensor carrier and retains the wave-guide sensor assembly in the installed position with the sensor probe being aligned with a drawing tube. The drawing tube terminates at a sample-container receiving portion that is shaped to releasably receive a sample container thereon.

The sample drawing device includes a drawing mechanism coupled to the drawing tube and adapted to draw a selected volume of a sample into the sample container for engagement with the wave-guide sensor during a sampling procedure. The sample drawing device includes an ejector coupled to the drawing mechanism and positioned adjacent to the drawing tube's sample container receiving portion. The ejector is movable between a retracted, disengaged position out of engagement with a sample container and an extended, ejection position to eject the sample container from the drawing tube's sample-container receiving portion. The tip ejector is adapted to selectively engage the drawing mechanism so activation of the drawing mechanism moves the ejector between the retracted, disengaged position and the extended, ejection position.

In another embodiment of the present invention, the sensor assembly is mounted on a sensor support device, such as a stand. The sensor is retained in a fixed position relative to the sensor support device and the probe cover is slidably movable

between a lowered, sensor-retracted position and a raised, sensor-exposed position to selectively expose the sensor probe during a sampling procedure. In a further embodiment, a plurality of sensor assemblies are mounted to a support device, for example, so the assemblies can be used simultaneously during a sampling procedure.

In one preferred embodiment of the present invention, the sample drawing device is a hand-held device having a handle, drawing mechanism, sensor-carrier-receiving portion, and testing electronics contained in a housing portion attached to the handle. The testing electronics include a power source, a microprocessor, an electromagnetic radiation source, a detection device, and a wave guide connecting cable adapted to connect the electromagnetic radiation source and detection device to the wave-guide-coupling member when the wave-guide sensor assembly is installed on the sample drawing device. A data display unit is attached to the handle and coupled to the detection device to display sampling results generated by the detection device for a selected sample. Accordingly, the hand-held sample drawing device, such as a pipette, is a self-contained testing unit.

In another embodiment of the present invention, the sample drawing mechanism is an automated drawing mechanism that allows for alternating positive and negative pressure within a drawing tube of the pipette. The alternating pressure within the drawing tube causes liquid sample within a pipette tip, which is connected to the pipette's drawing tube, to fluctuate or oscillate in the pipette tip between an upper level and a lower level. The sample oscillation within the pipette tip counteracts the creation of a concentration gradient within the sample during sensing. In an alternate embodiment, the sample drawing mechanism includes an adjustable air regulation system for controlling the amount of positive and negative pressure applied to the pipette tip.

In another embodiment of the present invention, the pipette has a removable, constricted pipette tip that is positioned in an operative relationship with the wave-guide sensor. In this embodiment, the pipette tip consists of a lower tip portion having a first cross-sectional area, an upper tip portion having a second cross-sectional area, and a constricted middle portion interposed between the lower and upper tip portions and having a third cross-sectional area that is less than either the first or second cross-sectional area of the respective lower and upper tip portions. The pipette tip is

sized so the sensor's sensing area is positioned in the constricted middle portion. The constricted middle portion provides for an accelerated sample flow over the sensor's sensing area as the sample is oscillated due to the venturi effect. Alternatively, the pipette tip consists of two-parts: a first tip-part and a second tip-portions removably attachable to the first tip-portion. The first tip-portion is a micropipette that is adapted to sample volumes of liquid ranging from 2 to 20 microliters inclusive.

In another embodiment of the present invention, the pipette is positioned in an operative relationship with the sensor and is adapted to allow the sensor's sensing area to move laterally within the pipette tip between first and second positions when the volume of a selected sample within the pipette is oscillated.

In an alternate embodiment, the sensor assembly includes a connecting member substantially adjacent to the sensor's input/output end, and the connecting member is attached to an elongated housing that contains the sensor therein. The connecting member has an engagement portion positioned to be engaged, automatically or manually, by the coupling member's sensor receiving portion. A distal end portion of the housing contains the sensor's sensing area therein and is adapted to allow sample to flow through the distal end portion and over the sensing area.

The present invention is also directed toward a method of analytically sampling a selected chemical sample with a wave-guide sensor assembly that is coupled to an analyzer and a source of electromagnetic radiation. The method of one embodiment of the invention includes providing a sensor carrier having a wave-guide receiving member that is coupled to the analyzer and the source of electromagnetic radiation by a wave-guide cable, removably attaching the wave-guide sensor to the wave-guide receiving member, and propagating electromagnetic radiation between the source of electromagnetic radiation and the sensing end portion of the wave-guide sensor through the wave-guide cable and the wave-guide sensor.

This embodiment of the sampling method also includes moving the wave-guide sensor relative to a sensor cover from a sensor contained position, in which the sensing end portion is covered by the sensor cover, to a sensor extended position, in which the sensing end portion is exterior of the sensor cover and exposed. The sample is then contacted with the sensing end portion of the wave-guide sensor. The

electromagnetic radiation propagating through the wave-guide cable from the sensing end portion of the wave-guide sensor is analyzed with the analyzer when the sensing end portion is contacting the sample, thereby analyzing the sample.

The method of one embodiment of the invention further includes the step of withdrawing the waveguide sensor from the sample and moving the wave-guide sensor from the sensor extended position to the sensor contained position with the sensing end portion being covered. After the waveguide sensor has been withdrawn to the sensor contained position, the waveguide sensor is moved to the sensor extended position, and sensing end portion is contacted with a second selected chemical sample.

In another alternate embodiment, the method includes the step of oscillating the sample within the pipette tip relative to the wave-guide sensor when the wave-guide sensor is in the sensor-extended position.

A method of another embodiment of the invention includes moving the selected chemical sample into contact with the sensing end portion of the wave-guide sensor and simultaneously analyzing with the analyzer the sample as it is moved into contact with the sensing end portion of the wave-guide sensor.

These and other aspects of this invention will become evident upon reference to the following detailed description and attached drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a partially exploded isometric view of a pipette and a wave-guide sensor assembly in accordance with a preferred embodiment of the present invention.

Figure 2 is an enlarged isometric view of the wave-guide sensor assembly of Figure 1, the wave-guide sensor assembly having a sensor carrier with a sensor coupling member slidably attached to a probe cover, and a fiber optic sensor connected to the sensor coupling member, the sensor coupling member being shown in solid line in a sensor-retracted position, and shown in phantom line in a sensor-extended position with the fiber optic sensor partially extending from the probe cover and shown in phantom line in an intermediate position between the sensor-retracted and sensor-extended positions.

Figure 3 is an enlarged cross-sectional view taken substantially along line 3-3 of Figure 2 showing the sensor carrier and the fiber optic sensor.

Figure 4 is an enlarged cross-sectional view taken substantially along line 4-4 of Figure 1 showing the fiber optic sensor.

Figure 5 is an isometric view of a protective storage housing removably containing the fiber optic sensor of Figure 4, with a closed-end tubular cover shown in phantom line.

Figure 6 is an enlarged cross-sectional view taken substantially along line 6-6 of Figure 5 showing the storage housing and the fiber optic sensor.

Figure 7 is an enlarged cross-sectional view taken substantially along line 7-7 of Figure 1 showing the pipette.

Figure 8 is a cross-sectional view of the pipette similar to Figure 7 with the sensor carrier of Figure 2 being shown in an installed position, a pipette tip being shown mounted on the pipette, the sensor coupling member and fiber optic sensor being shown in solid line in the sensor-extended position and shown in phantom line in the sensor-retracted position.

Figure 9 is a cross-sectional view of the pipette of Figure 8 with the sensor coupling member and fiber optic sensor shown in the intermediate position, a tip ejector of the pipette being shown in an ejection position, and the pipette tip being shown ejected from the pipette.

Figure 10 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a drawing mechanism operatively coupled to a pipette tip mounted on the pipette.

Figure 11 is an enlarged cross-sectional view of the pipette tip of Figure 10 shown with the sample level within the pipette tip at three different levels.

Figure 12 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a drawing mechanism operatively coupled to a pipette tip mounted on the pipette.

Figure 13 is a cross-sectional view of a constricted pipette tip of an alternate embodiment of the present invention, the pipette tip being shown mounted on the pipette.

Figure 14 is an enlarged cross-sectional view of a pipette tip of an alternate embodiment of the constricted pipette tip similar to the one shown in Figure 13, but with an elongated middle constricted portion.

Figure 15 is a cross-sectional view of a pipette tip of an alternate embodiment of the present invention, a two-part pipette tip being shown mounted on the pipette.

Figure 16 is a cross-sectional view of an alternate embodiment similar to the one shown in Figure 15, but with a shorter second tip-portion.

Figure 17 is a cross-sectional view of a pipette tip of an alternate embodiment of the present invention, the pipette tip being shown mounted on the pipette with the fiber optic sensor in the sensor-extended position and in a laterally off-set position, the sample level within the pipette tip being at an upper level.

Figure 18 is a cross-sectional view of the pipette tip of Figure 17 with the fiber optic sensor in the sensor-extended position and in an axially aligned position, the sample level within the pipette tip being at a lower level.

Figure 19 is a cross-sectional view taken substantially along line 19-19 of Figures 17 and 18 showing the fiber optic sensor in the lateral position and the axially-aligned position of Figure 17 and Figure 18, respectively.

Figure 20 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a fiber optic spectrograph contained in a housing portion and a data display on the pipette handle.

Figure 21 is a partial cross-sectional view of an alternate embodiment having a pipette regulating assembly with a piston that controls positive and negative pressure transmitted to the pipette tip.

Figure 22 is a partial cross-sectional view of an alternate embodiment having a pipette with a quick release sensor assembly and an adjustable regulating assembly with a piston and an adjustable stop to control the positive and negative pressure transmitted to the pipette tip.

Figure 23 is a partial cross-sectional view of an alternate embodiment having a pipette with regulating assembly with bellows that control the positive and negative pressure transmitted to the pipette tip.

Figure 24 is a cross-sectional view of the quick-release sensor assembly of Figure 23 with a sensor probe contained within a housing.

Figure 25 is a partial cross-sectional view of an alternate embodiment having a pipette with an electrochemical sensor thereon.

Figure 26 is a side elevation view of an alternate embodiment of the present invention showing a sensor assembly mounted on a stand.

Figure 27 is a side elevational view of an alternate embodiment of the present invention showing a sensor assembly mounted on a stand for automatic pipette positioning and automatic sample handling.

Figure 28 is an enlarged partial cross-sectional view of the sensor assembly of Figure 27.

Figure 29 is a side elevational view of an alternate embodiment with a plurality of sensor assemblies mounted on a support structure.

Figures 30A-F are left, right, front, rear, top, and bottom elevation views, respectively, of an alternate embodiment of the present invention.

Figure 31 is comparative experimental data for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10 and 11.

Figures 32A-C are comparative experimental data for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10, 11, and 13.

DETAILED DESCRIPTION OF THE INVENTION

The invention is directed toward a sensor assembly having a sensor carrier and a sensor therein that is usable in sampling a selected sample contacted by the sensor. The present invention is also directed toward a sample-drawing device, such as a pipette or the like, that releasably receives the sensor assembly for use during sampling or testing procedure.

In exemplary embodiments of the invention discussed herein, the sensor is a wave-guide sensor, although the invention also applies to other sensors, such as electrochemical sensors, surface acoustic sensors, transmission absorption sensors, and

the like. The wave-guide sensor is a fiber optic sensor removably connected to the wave-guide-sensor carrier for interchangeability with other fiber optic sensors. The wave-guide sensor carrier and fiber optic sensor are releasably received by the sample-drawing device and positionable to allow the fiber optic sensor to contact a sample drawn by the sample-drawing device. The wave-guide sensor assembly and sample-drawing device advantageously combine a wave-guide sensor with a sample-drawing device in a configuration that allows for inexpensive, fast, simple, accurate testing of selected samples with a high degree of repeatability.

A wave-guide sensor assembly 10 and a pipette 12 in accordance with a preferred embodiment of the present invention are shown in the figures for illustrative purposes. The pipette 12 releasably receives the wave-guide sensor assembly 10 therein and is adapted to draw a selected chemical sample, into a pipette tip 14 that removably attaches to a drawing tube 16 of the pipette 12. The wave-guide sensor assembly 10 is positioned and adapted to test the sample while the pipette tip 14 is on the pipette's drawing tube 16.

The wave-guide sensor assembly 10 includes a fiber-optic-sensor carrier 18 that is connected to a conventional fiber optic spectrograph 24 by a fiber-optic cable 22. The sensor carrier 18 releasably receives and optically couples a fiber optic sensor 20 to the fiber optic cable 22 and to the fiber optic spectrograph 24. The sensor carrier 18 moves the sensor 20 between a sensor-retracted position, wherein the sensor is protectively contained within the sensor carrier, and a sensor-extended position, wherein a portion of the sensor is exterior of the sensor carrier and exposed for a sampling procedure.

When the wave-guide sensor assembly 10 is installed on the pipette 12 and the sensor 20 is in the sensor-extended position, the sensor extends through the pipette's drawing tube 16 and a sensing area 28 of the sensor engages the sample drawn into the pipette tip 14. In the preferred embodiment, the sample is analyzed as the sample is being drawn into the pipette tip 14 while the pipette tip is on the pipette 12. The fiber optic spectrograph 24 is used to detect the characteristics of the sample contacted by the sensor's sensing area 28 by the propagation of multiple-wavelength

electromagnetic radiation through the sensor 20 and the fiber optic cable 22 between the sensor's sensing area 28 and the fiber optic spectrograph.

In the preferred embodiment, the sensor 20 is an SPR-based fiber optic sensor, although other wave-guide sensors are used with the sensor carrier 18 in alternate embodiments. The sensor carrier 18 includes an optical fiber coupling member 26 that releasably receives the sensor 20 and that is connected to the fiber optic cable 22. In one embodiment the coupling member 26 is permanently connected to the fiber optic cable 22, and in another embodiment the coupling member 26 is releasably connected to the fiber optic cable. The coupling member 26 coaxially aligns and operatively couples the sensor 20 to the fiber optic cable 22 to allow for efficient propagation of the electromagnetic radiation through the fiber optic cable and the sensor.

The pipette 12 of the preferred embodiment includes a carrier-receiving portion 30 that releasably receives the sensor carrier 18 in an installed position so the coupling member 26 and sensor 20 are coaxially aligned with the pipette's drawing tube 16. In an alternate embodiment, the sensor carrier 18 is integrally connected to the pipette 12. Accordingly, the pipette 12 and sensor carrier 18 form a unitary hand-held sampling device to which the fiber optic cable 22 and the sensors 20 attach for sampling of the sample.

The sensor carrier 18 includes a probe cover 32 that mounts into the pipette's carrier-receiving portion 30 and that slidably contains the carrier's coupling member 26. The coupling member 26 is slidable relative to the probe cover 32 and relative to the pipette 12 between a sensor-retracted position, wherein the sensor 20 is fully contained within the probe cover, and a sensor-extended position, wherein at least a portion of the sensor extends from the probe cover so the sensing area 28 is exterior of the probe cover to engage the selected sample.

The wave-guide sensor assembly 10 and pipette 12 of the present invention are usable for inexpensive, fast, efficient and highly repeatable sampling of selected chemical samples, while minimizing the amount of equipment and time needed and minimizing the risk of damage to the equipment. Further, the sensor 20 is easily removable from the coupling member 26 so different wave-guide sensors can quickly be

installed in the sensor carrier 18 for sampling different samples with a minimum amount of preparation time.

As best seen in Figures 2 and 3, the sensor carrier's probe cover 32 of the illustrated embodiment is a substantially cylindrical tube having an open top end 34, an open bottom end 36, and an interior area 38 extending therebetween that contains the carrier's coupling member 26. An end fitting 42 of the fiber optic cable 22 is attached to the coupling member 26 and the fiber optic cable extends through the probe cover's open top end 34.

The coupling member 26 includes a cylindrical body portion 40 fixedly attached to the cable's end fitting 42 and a threaded sensor-receiving portion 44 (Figure 3) coaxially aligned with the cable's end fitting. The threaded sensor-receiving portion 44 removably receives the sensor 20 therein and operatively couples the sensor to the fiber optic cable 22 with minimum signal loss or degradation.

The coupling member 26 also has a gripping portion 46 that is slidably positioned on the exterior of the probe cover 32. The gripping-portion is shaped and sized to be gripped by the fingers of a user for movement of the coupling member 26 between the sensor-retracted position, shown in solid line, and the sensor-extended position, shown in phantom line. The gripping portion 46 is securely attached to the coupling member's body portion 40 by a fastener 48 (Figure 3) that extends through an elongated slot 50 in the probe cover 32. The slot 50 extends partially between the open top and bottom ends 34 and 36 of the probe cover 32.

When the coupling member 26 is in the sensor-retracted position, it is adjacent to the probe cover's open top end 34, and the sensor 20 attached to the coupling member is fully contained within the probe cover 32 and protected from being damaged or inadvertently contaminated. When the coupling member 26 is in the sensor-extended position, the coupling member's body portion 40 is within the probe cover's interior area 38 adjacent to the open bottom end 36, and the threaded sensor-receiving portion 44 extends through the open bottom end and terminates at an end exterior of the probe cover 32. The sensor 20 attached to the coupling member 26 is also exterior of the probe cover 32 and ready for sampling the selected sample.

As the coupling member 26 moves between the sensor-retracted and sensor-extended positions, the coupling member's body portion 40 moves axially through the probe cover's interior area 38, and the gripping portion 46 slides along the outside surface of the probe cover.

The probe cover 32 has detent apertures 52 adjacent to the elongated slot 50 near the probe cover's open top and bottom ends 34 and 36. The detent apertures 52 are releasably engaged by the gripping portion 46 of the coupling member 26 to positively retain the coupling member in the respective sensor-retracted and sensor-extended positions. The coupling member's body portion 40 and the gripping portion 46 also frictionally engage the probe cover 32. Accordingly, the coupling member 26 and the sensor 20 attached thereto will remain in any selected position between the sensor-retracted and sensor-extended positions, so the coupling member and the sensor will not inadvertently drop to the sensor-extended position.

The probe cover 32 of the preferred embodiment also has a set of intermediate detent apertures 54 adjacent to the elongated slot 50 at an intermediate position between the other detent apertures 52. The intermediate detent apertures 54 releasably retain the coupling member 26 and the sensor 20 in the intermediate position, shown in phantom line in Figure 3 between the sensor-retracted position and the sensor-extended position. When the wave-guide sensor assembly 10 is installed on the pipette 12 and the coupling member 26 and sensor 20 are in the intermediate position, the sensor's sensing area 28 is fully contained within the pipette's drawing tube 16 so the drawing tube protects the sensing area from damage or inadvertent contamination. Therefore, the sensor's sensing area 28 is protected when the wave-guide sensor assembly 10 is installed on the pipette 12 and the coupling member 26 is in either the sensor-retracted position, the intermediate position, or any position therebetween.

When the wave-guide sensor assembly 10 is removed from the pipette 12, the coupling member 26 and the sensor 20 are in the sensor-retracted position, as discussed in greater detail below, so the sensor's sensing area 28 is protected from damage or inadvertent contamination.

As best seen in Figure 4, the preferred SPR-based fiber optic sensor 20 includes a probe 56 formed by a solid core wave guide 58 comprising the fiber optic

core, fiber optic cladding layer 60, and fiber optic buffer layer 61 which extends from an input/output end 66 and terminates at a terminal reflection end 62. The buffer layer 61 and cladding layer 60 are removed exposing the core for a selected length. Deposited around the exposed core is a layer of an SPR supporting metal forming the sensing area 28. The terminal reflection end 62 is defined by an end face of the core wave guide 58 in contact with a reflective layer 64 that does not support SPR.

The core wave guide's input/output end 66 receives the electromagnetic radiation propagated through the fiber optic cable to the sensor, and the electromagnetic radiation propagates to the terminal reflection end 62 by total internal reflections in the core wave guide 58. The electromagnetic radiation is reflected off the reflective layer 64 in contact with the end face of the core wave guide 58, and propagates back down the core wave guide by the total internal reflections to the input/output end 66. The fiber optic spectrograph's detection device monitors the electromagnetic radiation entering and exiting the input/output end 66 of the core wave guide 58 to determine the results of the selected test or sampling.

The sensor 20 includes a threaded connecting member 68, preferably formed by an injection molded, substantially rigid plastic that is attached to the fiber optic probe 56 adjacent to the input/output end 66. The connecting member 68 has external threads sized to threadably connect to the coupling member's sensor-receiving portion 44 (Figure 3) by being screwed into the sensor-receiving portion. As the sensor's connecting member 68 is screwed into a fully engaged position, the input/output end 66 of the fiber optic probe 56 is positioned immediately adjacent to and coaxially aligned with the end fitting 42 of the fiber optic cable 22 to allow propagation of the electromagnetic radiation into and out of the fiber optic probe. Accordingly, the fiber optic probe 56 is easily and quickly coupled to the fiber optic cable 22 by screwing the sensor's connecting member 68 into the sensor-receiving portion 44 of the coupling member 26.

As best seen in Figure 4, the connecting member 68 of the preferred embodiment is secured to the fiber optic probe 56 by crimping the connecting member onto the buffer layer 61. As the connecting member 68 is crimped onto the buffer layer 61, the end of the connecting member 68 is flush with the end of the core wave guide 58.

Accordingly, the input/output end 66 of the core wave guide 58 is substantially coplanar with the end of the connecting member 68 for efficient propagation of light through the fiber optic probe 56 with a minimum degree of signal loss.

In an alternate embodiment, the input/output end 66 of the core wave guide 58, which is a silicon wave guide, is recessed within the buffer layer 61 by approximately 100 microns. The end of the buffer layer 61 abuts the end fitting 42 of the fiber optic cable 22, and the silicon wave guides are out of direct engagement with each other. The recessed input/output end 66 of the sensor 20 still provides an efficient coupling between the fiber optic cable and the sensor.

In another alternate embodiment, the sensor 20 is a bare fiber sensor without the connecting member 68 at the input/output end. The coupling member 26 in this alternate embodiment is a bare fiber coupler that removably receives the input/output end of the sensor and aligns the sensor's core wave guide with the fiber optic cable 22 for efficient propagation of electromagnetic radiation between the fiber optic cable and the sensor.

When the sensor 20 is not installed on the coupling member 26 (Figure 3), the sensor 20 is stored in a protective storage housing 72 illustrated in Figure 5. The storage housing 72 is a substantially cylindrical tube shaped and sized to fully contain the sensor 20 therein and to protect the sensor's connecting member 68 and sensing area 28 from being inadvertently impacted, damaged, or contaminated. The storage housing 72 is open at both ends so the storage housing and sensor 20 can be packaged as a unit, for example, in a nitrogen gas environment or other selected environment that is best for protecting and storing the sensor before it is used.

The storage housing 72 of the preferred embodiment is a plastic tube that is adapted to be color coded by labels or by forming the storage housing from a plastic material of a selected color. Such color coding of the storage housing 72 allows different types of sensors 20 having different sensing characteristics to be contained in different colored storage housings for easy identification of the sensors.

As best seen in Figures 5 and 6, the storage housing 72 includes an interior flange 74 extending across the housing's interior area near one end of the housing. The interior flange 74 has a central aperture 76 that receives the fiber optic

probe 56 therethrough, and a hexagonal-shaped recessed portion 78 is formed around the central aperture. The recessed portion 78 is sized to receive a mating hexagonal flange 70 on the sensor's connecting member 68 so the hexagonal flange 70 snaps into the recessed portion and into engagement with the storage housing's flange 74. Accordingly, the interior flange 74 releasably retains the sensor 20 within the storage housing 72.

The storage housing 72 is sized to fit into the carrier's probe cover 32 (Figure 3) and to position the connecting member 68 adjacent to the sensor coupling member 26. Installation of the sensor 20 is performed by placing the storage housing 72 with the sensor 20 therein into the probe cover's interior area 38 until the threaded portion of the sensor's connecting member 68 partially engages the receiving portion 44 of the coupling member 26. The storage housing 72 and the sensor 20 are then rotated as a unit, whereby the sensor's connection member 68 is screwed into engagement with the receiving portion 44. The hexagonal-shaped recess 78 in the storage housing 72 acts as a wrench mechanism that engages the connecting members hexagonal flange 70 for easy installation of the sensor 20 into the coupling member 26 to ensure secure engagement and proper alignment of the sensor. After the sensor 20 has been screwed into the installed position, the storage housing 72 is pulled out of the probe cover 32 so the sensor's hexagonal flange 70 is pulled out of the hexagonal recess 78 of the storage housing's flange 74.

The storage housing 72 of the preferred embodiment has a step configuration with a narrower end portion 81 adjacent to the sensing area 28 when the sensor 20 is contained in the housing and a wider end portion 83 adjacent to the sensor's connecting member 68. This step configuration allows a closed-end tube 85, shown in phantom lines in Figure 5, to be mounted onto the narrower end portion 81 so as to cover and close-out the one end of the storage housing 72. The closed-end tube 85 provides additional protection for the sensor 20 and allows the sensor's sensing area 28 to be stored in a selected liquid environment when the sensor is not in use.

As best seen in Figure 5, the narrower end portion 81 of the storage housing 72 has a plurality of rib portions 80 around the exterior of the storage housing. These rib portions 80 provide a gripping surface on the exterior of the storage housing

72 to facilitate rotation of the storage housing and the sensor for installation and removal of the sensor.

In an alternate embodiment, the storage housing 72 is an elongated tubular member with a substantially constant outer diameter, and the storage housing does not have the step configuration. This non-step configuration is easy and inexpensive to manufacture. The end of the storage housing 72 opposite the interior flange 74 is provided with the rib portions 80 to form the gripping surface.

The sensor 20 is removed from the coupling member 26 by moving the storage housing 72 into the probe cover's interior area 38 over the fiber optic probe 56, and pressing the storage housing's flange 74 against the sensor until the hexagonal flange 70 snaps into the hexagonal recess 78. The storage housing 72 and the sensor 20 are then rotated as a unit, the sensor fully unscrewed from the coupling member, and the storage housing and sensor removed as a unit from the probe cover 32. The carrier's coupling member 26 is then ready to receive a different sensor 20. Accordingly, a first sample may be sampled with one sensor when in the sensor-extended position. The sensor is then withdrawn to the sensor-retracted position, removed from the coupling member, and a second sensor is installed for sampling other samples. This replacement of sensors 20 is a very quick and easy procedure.

While the preferred embodiment of the wave-guide sensor assembly 10 is described with respect to the fiber optic sensor 20 coupled to the fiber optic cable 22, the present invention is also applicable to other wave-guide sensors, such as planar wave-guide sensors or the like, usable with a wave guide cable and with an electromagnetic radiation source for propagation of the electromagnetic radiation to and from the wave-guide sensor. In addition, the preferred embodiment utilizes the threadable engagement between the sensor 20 and the coupling member 26, although other interconnections between the sensor and the coupling member such as the bare fiber couplers are available to quickly, easily, and efficiently couple the sensor with the fiber optic cable 22.

As best seen in Figure 7, the pipette 12 of the preferred embodiment is a hand-held sampling device that includes the carrier-receiving portion 30 that is defined by a concave semicylindrical surface integrally formed in a pipette handle 100. The

handle 100 has a bottom portion 102, which defines a bottom end of the carrier-receiving portion 30, and a top portion 104, which defines the upper end of the carrier-receiving portion. A main body portion 106 of the handle 100 extends between the top and bottom portions 104 and 102, and the concave semicylindrical surface is formed in the handle's body portion.

The drawing tube 16 projects away from the handle's bottom portion 102 from a surface opposite the carrier-receiving portion 30. The handle's bottom portion 102 has a sensor-assembly receiving aperture 108 therein open to the carrier-receiving portion 30 and connected to an interior passageway 110 extending through the drawing tube 16. The sensor-assembly receiving aperture 108 is coaxially aligned with the interior passageway 110 and the carrier-receiving portion 30.

The pipette 12 has a drawing mechanism 112 extending through the handle 100 and operatively coupled to the drawing tube 16 to create a selected partial vacuum within the interior channel 110 for drawing a selected volume of a sample into the pipette tip 14 (Figure 1) mounted on the drawing tube 16. In an alternate embodiment, the drawing mechanism 112 is a sample handling device that also creates a selected positive pressure within the interior channel 110 for moving the sample axially in the pipette tip 14 away from the drawing tube 16, and if desired out of the pipette tip 14. Accordingly, the drawing mechanism is broadly defined herein as a device that generates negative and positive pressures that move the sample axially in the pipette tip14. The drawing mechanism 112 has an adjustable thumb-actuated plunger 114 that projects through the handle's top portion 104 and connects to an interior piston 116 that is slidably positioned within a cylinder 120 formed in the handle's body portion 106. The plunger 114 is ergonomically positioned so that a user grasping the handle's body portion 106 can easily and comfortably access the plunger with his or her thumb in order to depress the plunger from a raised position to a lowered position.

The interior piston 116 has a lower engaging surface 128 that engages a flat head 126 of a rod 122, and the rod slidably extends into a suction aperture 124 formed in the handle's bottom portion 102. The rod 122 extends through a piston-biasing spring 130 that is positioned between the rod's flat head 126 a lower seat portion 132 formed in the handle's body portion 106. Accordingly, the piston-biasing spring

130 biases the rod 122 and the interior piston 116 away from the handle's bottom 102 portion, thereby pressing the plunger 114 toward the raised position.

A seal member 134 is provided at the upper end of the suction aperture 124, and the seal member sealably engages the rod 122. The seal member 134 prevents air within the suction aperture 124 from exiting through the suction aperture's upper end when the interior piston 116 presses the rod 122 into the suction aperture upon depression of the plunger 114. A connecting passageway 136 interconnects the suction aperture 124 with the interior channel 110 at the sensor-assembly receiving aperture 108 to allow the air to exit or enter the suction aperture.

Air is pushed out of and drawn into the suction aperture 124 by moving the rod 122 axially within the suction aperture, which is achieved by pumping the plunger 114 so as to axially move the interior piston 116 within the cylinder. Because the sensor-assembly receiving aperture 108 in the handle's bottom portion 102 communicates with the carrier-receiving portion 30 a significant suction will only be generated in the drawing tube 16 when the sensor-assembly receiving aperture 108 is fully sealed. When the sensor-assembly receiving aperture 108 is sealed, the only path for air to move into and out of the suction aperture is through the connecting channel 136 and the interior channel 110 within the drawing tube 16. As discussed in detail below, the wave-guide sensor assembly 10 is adapted to fully seal the sensor-assembly receiving aperture 108 to allow for accurate and controlled suction within the drawing tube when the plunger 114 is pumped.

As best seen in Figure 8, the carrier-receiving portion 30 removably receives the wave-guide sensor assembly 10 in an installed position. When the wave-guide sensor assembly 10 is in the installed position, the open bottom end 36 of the probe cover 32 is received in a recess 140 formed in the handle's bottom portion 102 around the sensor-assembly receiving aperture 108. The probe cover's open top end 34 is immediately adjacent to the handle's top portion 104 so the probe cover 32 is coaxially aligned with the sensor-assembly receiving aperture 108 and the drawing tube 16 in the handle's bottom portion 102. The carrier's coupling member 26 slides between the handle's top and bottom portions 104 and 102. Accordingly, the coupling member's

body portion 40 and sensor-receiving portion 44 are also coaxially aligned with the sensor-assembly receiving aperture 108 and the drawing tube 16.

When the coupling member 26 is in the sensor-retracted position, the sensor-receiving portion 44 is positioned within the probe cover 32 generally adjacent to the handle's top portion 104 and away from the sensor-assembly receiving aperture 108. A sensor 20 that is installed on the coupling member 26 is also positioned fully within the probe cover 32 and spaced away from the sensor-receiving aperture 108, so the sensor is protected from damage or contamination. When the coupling member 26 is in the sensor-extended position, the sensor-receiving portion 44 extends into the sensor-assembly receiving aperture 108. The probe 56 of the installed sensor 20 extends through the drawing tube 16 with the sensing area 28 exterior of the drawing tube and ready to engage the selected sample.

An O-ring seal 141 is mounted on the sensor receiving portion 44 and is positioned to sealably engage the walls of the sensor-assembly receiving aperture 108 when the coupling member 26 is in the sensor-extended position. The O-ring seal 141 blocks the passage of air through the upper end of the sensor-assembly receiving aperture 108 so the only passageway for air into and out of the suction aperture 124 is through the drawing tube 16. Therefore, the pipette 12 of the preferred embodiment creates drawing suction through the drawing tube 16 only when the wave-guide sensor assembly 10 is in the installed position and the coupling member 26 is in the sensor-extended position. The suction is created whether or not the sensor 20 is connected to the coupling member 26.

When a user depresses the plunger 114, the plunger moves the interior piston 116 downwardly thereby moving the rod 122 downwardly into the suction aperture 124, which forces air out of the suction aperture through the connecting channel 136. When the plunger 114 is released, the biasing spring 130 moves the rod 122 upwardly within the suction aperture 124, thereby creating suction within the suction aperture 124 that draws air from the drawing tube's interior channel 110, through the connecting channel 136, and into the suction aperture. The amount of suction created is controlled by regulating the stroke length or distance traveled by the rod 122 within the suction aperture 124 when the plunger 114 is depressed and released.

When the pipette tip 14 is retained on the drawing tube, placed into a sample, and plunger 114 is depressed and released, suction is generated within the pipette tip so as to draw the sample into the pipette tip. When the sensor 20 is connected to the coupling member 26, the sensor's sensing area 28 extends into the pipette tip 14. As the sample is drawn into the pipette tip 14, the sample is also drawn into engagement with the sensing area 28 for quick, easy, and accurate measurements.

In the preferred embodiment, the plunger 114 is connected to the interior piston 116 by a plunger shaft 138 that threadably receives the plunger 114. The stroke length of the rod 122 is controlled by adjusting the position of the plunger 114 on the plunger shaft 138. The further the plunger is screwed onto the plunger shaft 138, the shorter the stroke length of the rod 122, thereby resulting in less suction within the drawing tube 16.

As best seen in Figure 1, coupling member 26 is releasably located in the sensor-extended position when the wave-guide sensor assembly 10 is installed on the pipette 12. The body portion 106 of the pipette's handle 100 has a grip-receiving portion 142 adjacent to the carrier-receiving portion 30 and also adjacent to the handle's bottom portion 102. The grip-receiving portion 142 is positioned and sized to releasably receive the gripping portion 46 of the coupling member 26 in a locked position when the coupling member is in the sensor-extended position and the probe cover 32 rotated about its central axis toward the grip-receiving portion. The grip-receiving portion 142 has an upper endwall 143 that blocks the gripping portion 46 from sliding away from the handle's bottom portion 102 when in the locked position. Accordingly, the grip-receiving portion 142 provides a locking feature that releasably locks the coupling member 26 in the sensor-extended position to prevent inadvertent upward movement of the sensor 20 during a sampling procedure.

The gripping portion moves to an unlocked position when the probe cover 32 and coupling member 26 are rotated as a unit away from the grip-receiving portion 142. In the unlocked position, the gripping portion 46 is movable upwardly toward the handle's top portion 104 so as to slide the coupling member toward the sensor-retracted position.

In the preferred embodiment, the gripping portion 46 has a semicylindrical inner surface that extends around the probe cover 32. Edges of the gripping portion 46 are immediately adjacent to the edges of the handle's body portion 106 at the carrier-receiving portion 30, so rotation of the coupling member 26 and probe cover 32 is restricted by the edges of the handle's body portion. Accordingly, the coupling member 26 and probe cover 32 are rotatable relative to the pipette 12 only when the gripping portion 46 is positioned adjacent to the grip-receiving portion 142 or another grip-receiving area formed in the handle 100.

As best seen in Figures 1 and 8, the pipette 12 has a carrier-lock member 145 connected to the handle's top portion 104 and adapted to releasably lock the wave guide-sensor assembly 10 in the installed position. The carrier-lock member 145 includes a pair of biased retaining arms 144 that extend into the carrier-receiving portion 30 and releasably engage the open top end 34 of the probe cover 32 when the wave-guide sensor assembly 10 is in the installed position. The retaining arms 144 each have an engaging tab 146 that extends over the edge of the probe's open top end 34 and abuts the sidewall of the probe cover 32 so as to block the probe cover from inadvertently moving away from the handle 100 and out of the carrier-receiving portion 30.

The carrier-lock member 145 is moved to an unlocked position by sliding the coupling member 26 upwardly, past the sensor-retracted position and pressing the gripping portion 46 into engagement with the engaging tabs of the retaining arms 144. The gripping portion 46 moves the retaining arms 144 upwardly so the retaining tabs 146 are out of engagement with the probe cover 32. The probe cover 32 and the coupling member 26 are then moved as a unit away from the pipette's carrier-receiving portion 30. Accordingly, the wave-guide sensor assembly 10 is removed from the pipette 12 only when the coupling member 26 and the sensor 20, if installed, are in the sensor-retracted position.

The top portion 104 of the pipette's handle 100 has a U-shaped cable-receiving groove 148 that receives the fiber optic cable 22 therethrough when the wave-guide sensor assembly 10 is in the installed position. The cable-receiving groove 148 allows the fiber optic cable 22 to move with the coupling member 26 between the sensor-retracted and sensor-extended positions without binding or bending the fiber

optic cable past a predetermined minimum bend radius so as to maintain efficient propagation of the electromagnetic radiation through the fiber optic cable.

As best seen in Figures 8 and 9, the pipette 12 has a tip ejector 150 connected to the handle 100 that is adapted to eject the pipette tip 14 from the end of the drawing tube 16. The tip ejector 150 has an ejector tube 152 movably positioned adjacent to the pipette's drawing tube. The ejector tube 152 concentrically surrounds the drawing tube 16 and extends away from the handle's bottom portion 102 and terminates at an ejector surface 153. The ejector surface 153 is spaced apart from the end of the drawing tube 16 to allow the pipette tip 14 to extend over and releasably engage an exposed portion of the drawing tube. The pipette tip 14 terminates at a position adjacent to the ejector surface 153 when the tip ejector 150 is in a retracted, disengaged position, shown in Figure 8. The tip ejector 150 is movable to an extended, ejection position, shown in Figure 9, wherein the ejector surface 153 moves toward the end of the drawing tube 16, engages the pipette tip 14, and pushes the pipette tip off the drawing tube 16.

The tip ejector 150 has an ejector foot 154 that supports the ejector tube 152 and that is movably received within a recess in the handle's bottom portion 102. An ejector rod 156 is securely connected at its bottom end to the ejector foot 154 and extends upwardly through the handle's bottom portion 102, and terminates at an ejector head 158 positioned within the handle's body portion 106. The tip ejector 150 is biased toward the retracted, disengaged position by a biasing spring 159 that is slightly compressed between the bottom of the ejector head 158 and the handle's bottom portion 102. The ejector tube 152 is moved to the extended, ejection position to eject the pipette tip 14 when an ejection force is exerted on the ejector head 158 and the ejector rod 156 moves away from the handle's body portion 106, thereby causing the ejector foot 154 and the ejector tube to move relative to the drawing tube 16 to the extended, ejection position.

The tip ejector 150 includes an ejector piston 160 engaging the ejector head 158 and being slidably positioned within the handle's cylinder 120. The ejector piston 160 is positioned adjacent to the interior piston 116, and a movable activation blade 164 positioned to releasably engage the interior piston extends away from the

ejector piston. The activation blade 164 is slidably engaged by an activation pin 166 that extends through an aperture 168 in the handle's body portion 106 and partially into the carrier-receiving portion 30. The tip ejector 150 is activated by depressing the activation pin 166, as discussed in greater detail below, and then depressing the pipette's plunger 114, resulting in ejection of the pipette tip 14.

The activation blade 164 is movable between a disengaged position wherein it is out of engagement with the interior piston 116, illustrated in Figure 8, an activating position engages the interior piston. The activation blade 164 is biased toward the disengaged position, which presses the activation pin 166 partially into the carrier-receiving portion 30. When the activation blade 164 is in this disengaged position and the user depresses the plunger 11, the interior piston 116 does not engage the activation blade 164 as the interior piston moves toward the handle's lowered position. Accordingly, tip ejector 150 is not moved to the extended, ejection position and it remains in the retracted, disengaged position. When the activation pin 166 is pressed toward the interior piston 116, the activation blade 164 moves to the activating position and into engagement with the interior piston. Movement of the interior piston 116 toward the housing's bottom portion 102 causes the activation blade 164 and the ejector piston 160 to simultaneously move, thereby moving the ejector foot 154 and the ejector tube 152 to the extended, ejection position.

As best seen in Figures 8 and 9, movement of the activation pin 166 and the activation blade 164 relative to the interior piston 116 is controlled by the rotational position of the probe cover 32 when the wave-guide sensor assembly 10 is in the installed position. The probe cover 32 has an elongated ejector slot 168 positioned to receive the activation pin 166 when the coupling member 26 is in the sensor-retracted position and the sensor-extended position. As the coupling member 26 slides between the sensor-retracted position and the sensor-extended position, the activation pin 166 remains protruding through the ejector slot 168 so the tip ejector 150 will not move as the user depresses the plunger 114. The ejector slot 168 is also sized to receive the activation pin 166 when the probe cover 32 and coupling member 26 are rotated relative to the pipette 12, when the coupling member 26 is in the sensor-extended position, to the locked position.

The probe cover 32 and the coupling member 26 are also rotatable relative to the pipette 12 in the opposite direction when in the intermediate position. However, the activation pin 166 does not remain in the ejector slot 158, so the activation pin is pressed toward the interior piston 116, thereby moving the activation blade 164 into engagement with the interior piston for activation of the tip ejector by the user upon depressing the plunger 114. As best seen in Figure 1, the housing's body portion 106 has an intermediate grip-receiving portion 170 formed therein at a position corresponding to the intermediate position of the coupling member 26. The intermediate grip-receiving portion 170 is adjacent to the carrier-receiving portion 30 and on the opposite side from the lower grip-receiving portion 142. In the intermediate position, the sensor's sensing area 28 is contained and protected within the drawing tube 16.

When the coupling member 26 is in this intermediate position, shown in Figure 9, the probe cover 32 and coupling member 26 are rotatable as a unit so the gripping portion 46 moves into the intermediate grip-receiving portion 170. As the probe cover 32 rotates toward the intermediate grip-receiving portion 170, the probe cover's ejector slot 168 is rotated away from the activation pin 166 thereby causing the exterior surface of the probe cover 32 to press the activation pin 166 inwardly toward the interior piston 116, which moves the activation blade 164 into engagement with the interior piston 116. The tip ejector 150 is then ready to eject the pipette tip 14 upon depressing the plunger 114.

In the preferred embodiment, the activation blade 164 moves into engagement with the interior piston 116 for activation of the tip ejector 150 only when the interior piston 116 is in the raised position, when the coupling member 26 is in the intermediate position, and when the gripping portion 46 rotated into the intermediate grip-receiving portion 170. As the probe cover 32 presses the activation pin 166 inwardly, the activation blade 164 is moved into engagement with the interior piston 116, as shown in Figure 9, and the tip ejector 150 ejects the pipette tip 14 upon depressing the plunger 114.

The plunger 114 presses the interior piston 116, the activation blade 164, and the ejector piston 160 downwardly, which moves the ejector rod 156, the ejector foot 154, and the ejector tube 150 to the extended, ejection position and pushes the

pipette tip 14 off of the drawing tube 16. Accordingly, the user can eject the pipette tip 14 into a suitable waste receptacle after sampling a selected sample without the user ever having to touch the pipette tip and risking contamination of the user's hand or the equipment used during the sampling procedure. A new pipette tip 14 is then attached to the drawing tube 16, the sensor 20 is then moved to the sensor-extended position, a sample is drawn into the new pipette tip 14 and into engagement with the sensor's sensing end 28.

If an initial analysis of a sample is not sufficiently complete, the sensor 20 can also be withdrawn from the pipette tip 14, moved to the intermediate position, and then reintroduced into the pipette tip 14 for additional analysis. If the sample does not need further analysis, the pipette tip 14 is ejected when the sensor 20 is in the intermediate position, a new pipette tip is installed on the pipette drawing tube, and the sensor is moved to the sensor-extended position. Another sample is drawn into the pipette tip 14 and is analyzed as the sample contacts the sensor's sensing area 28. After the sample has been analyzed, the sensor 20 is moved to the sensor-retracted position or the intermediate position to cover and protect the sensing area 28 from being inadvertently impacted, contaminated, or otherwise damaged.

In the preferred embodiment, the pipette tip 14 that is used with the pipette 12 and the wave-guide sensor assembly 10 has a generally conical-shaped sidewall that defines an open top end sized to partially fit over the drawing tube 16 and an open bottom end with a small opening through which the selected sample is drawn into the pipette tip.

In another embodiment, the same embodiment above is used where the pipette tip's sidewall also defines an interior surface that communicates with the selected sample drawn into the pipette tip. The pipette tip's interior surface is coated with a selected chemical treatment that is utilized during a sampling procedure. The selected chemical treatment, forming a surface coating on the inside wall of the pipette tip 14, provides a means for preparation of a specific surface for solid-phase reaction, for biologically active surfaces, for surfaces preactivated for subsequent coupling reactions, or for further functionalization or derivatization. The selected chemical treatment can be a duplicate of the chemistry on the sensor tip or may optionally be an alternative

chemistry, depending on the application. The surface coating of one embodiment provides an additional surface area to extend the binding capacity and thus separation of selective chemical or biochemical agents from the bulk solution contained in the pipette tip 14. The selected surface coating also allows the pipette tip 14 to be used in containing, concentrating, purifying and/or transporting selective chemical or biochemical agents, such as for use in other chemical/biochemical processing (i.e., further purification, PCR, further interaction analysis studies) or chemical analysis (i.e., mass spectrometry, etc.)

Use of the sensor 20 and pipette tip 14 with the selected surface coating for direct analysis and simultaneous handling of the agent for processing, as discussed above, results in the advantages of time savings, qualities in results, etc. For example, in such an application, the selective chemistry on the sensor tip and the modified inside wall of the pipette tip 14 can bind a specific chemistry on the sensor tip and the modified inside wall of the pipette tip can bind a specific chemical agent, the sensor response thus confirming the specificity. The agent may then, under selected chemical conditions, be washed off from the pipette tip wall and the sensor into a container for further processing.

In one embodiment, the pipette tip is a finned-pipette tip that has a plurality of fins extending radially inwardly from the sidewall toward the axis of the pipette tip. The fins provide an increased surface area within the pipette tip that is available to contact the selected sample. These fins are also coated with the selected chemical treatment so the surface area of the chemical treatment within the finned-pipette tip that is available to contact the selected sample is greater than the available surface area of a non-finned pipette tip. In other embodiments, the increased surface area in the pipette tip is provided by a hydrogel layer or a layer of small porous particles that are chosen for use with selected sensors in selected sampling processes.

In one embodiment, the sample drawn into the pipette tip is agitated or stirred to provide movement of the sample relative to the probe's sensing area. Such movement or hydrodynamic agitation of the sample provides an increased mass transport of the chemical or biochemical species in the sample to the sensor area achieving accurate measurements and avoiding static conditions. Such movement or

hydrodynamic agitation of the sample in the pipette tip 14 may be achieved by providing a piezoelectric stirrer or other mixing devices that cycle into and out of the pipette tip. Movement may also be achieved by moving or vibrating the probe 56 when it is extended into the pipette tip 14 and into the sample.

Difficulties in mass transport in some testing procedures may be associated with static hydrodynamic conditions within the pipette tip 14. Such mass transport difficulties may be overcome by oscillating the sample level within the pipette tip 14. As best seen in Figure 10, an alternate embodiment of the present invention includes a drawing mechanism 300 that is operatively coupled to the pipette's drawing tube 16 to create selected negative and positive pressures within the drawing tube's interior passageway 110 and in the pipette tip 14 when the pipette tip is installed. Negative pressure is used to draw a sample into the pipette tip 14, and the pressure is then oscillated between selected positive and negative pressures to axially oscillate the sample within the pipette tip. The drawing mechanism 300 in one embodiment is an automated drawing mechanism that is used in lieu of the manual drawing mechanism 112 (Figure 8) described earlier. The automated drawing mechanism 300 preferably includes a conventional reciprocating pump consisting of a piston within a cylinder, wherein the piston has specific static positions, as well as different frequencies and stroke amplitudes. In this configuration, the volume of air or other gas introduced and expelled from the drawing mechanism 300 is highly controlled by controlling the frequency and stroke amplitude, thereby allowing for highly controlled oscillation of the sample within the pipette tip 14.

The drawing mechanism 300 is operatively connected to the pipette 12 by a hydraulic or pneumatic tube 302. One end 301 of the tube 302 is connected to a tube connector 304 on the bottom portion 102 of the pipette handle. The tube connector 304 has an air passageway 305 that communicates with the suction aperture 124 in the pipette handle's bottom portion 102. The connecting passageway 136 in the bottom portion 102 interconnects the suction aperture 124 with the drawing tube's interior channel 110 at the sensor-assembly receiving aperture 108 to allow air or other selected gas, such as nitrogen, to exit or enter the drawing tube's interior channel and the pipette tip 14. When the wave-guide sensor assembly 10 is in the installed position, the drawing

mechanism 300 generates the alternating positive and negative pressure in the pneumatic tube 302, the tube connector 304, the suction aperture 124, the connecting passageway 136, and the drawing tube 16, thereby causing oscillating pressures within the drawing tube and the pipette tip 14.. Accordingly, the alternating pressures cause the sample level within the pipette tip 14 to rise and fall in a controlled and oscillatory manner.

In operation, the drawing mechanism 300 generates a negative pressure in the pipette tip 14 while the pipette tip is inserted into a sample, thereby drawing a selected volume of the sample into the pipette tip. As best seen in Figure 11, the sample's upper level within pipette tip 14 after the sample is first taken is at an initial upper position AH, and the sample's lower level is at a lower position AL at the lower end of the pipette tip. When the fiber optic probe 56 is in the sensor-extended position with the sensing area 28 in the sample, the drawing mechanism 300 is activated and generates the alternate positive and negative pressures within the pipette tip 14.

When the drawing mechanism 300 generates the negative pressure during a suction phase, the sample's upper and lower levels move axially relative to the probe's sensing area 28 toward the pipette's drawing tip 16 to raised upper and lower positions CH and CL, respectively, shown in phantom lines. When the drawing mechanism 300 generates the positive pressure during a pressure phase, the sample is moved axially away from the drawing tip 16 so the sample's upper level moves from the raised upper level CH to a lowered upper level BH, shown in phantom lines. The sample's lower level moves from the raised lower level CL to the end of the pipette tip 14. If the positive pressure is sufficient, a small amount of the sample is expelled from the pipette tip during the pressure phase. The sample's oscillatory movement within the pipette tip 14 relative to the probe's sensing area 28 causes a forced convective flow around the sensing area, thereby counteracting the creation of a concentration gradient within the sample.

As best seen in Figure 12, an alternate embodiment includes the pneumatic tube 302 that extends through the pipette handle 100 and connects to an air passageway 350 in the handle's bottom portion 102. The air passageway 350 communicates with the suction aperture 124 and is positioned above the connecting channel 136. Accordingly, the air passageway 350 is coupled to the drawing tube's

interior passageway 110 via the suction aperture 124 and the connecting channel 136. In another alternate embodiment, the pneumatic tube 302 is positioned along the exterior of the pipette handle's main body portion 106 and connects to a connection port 351 in the handle's bottom portion 102. The connection port 351 is connected to the air passageway 350 so as to operatively connect the pneumatic tube 302 to the air passageway. In each of these alternate embodiments, the pneumatic tube 302 is operatively coupled to the drawing tube's interior channel 110, and thus to the interior of the pipette tip 14, so as to allow the positive and negative pressures to be transmitted to the pipette tip for sample oscillation relative to the sensing area 28.

As best seen in Figure 13, an alternate embodiment of the present invention includes a pipette tip 14 that is partially constricted at a position below the pipette's drawing tube 16. The partially constricted pipette tip has a lower portion 14a, a constricted middle portion 14b, and an upper portion 14c. The constricted middle portion 14b is generally adjacent to the sensing area 28 when the probe 56 is in the sensor-extended position, and has a cross-sectional area that is smaller than the cross-sectional areas of the lower portion 14a and the upper portion 14c. The constricted middle portion 14b has a length that substantially corresponds to the length of the probe's sensing area 28, and the middle portion is positioned to contain substantially all of the sensing area when the probe is in the sensor-extended position. As such, the pipette tip 14 behaves as a venturi, so the sample flow rate within the pipette tip 14 during sample oscillation increases as the sample moves through the constricted middle portion 14b. The increased flow rate of sample next to the probe's sensing area 28 significantly reduces drawbacks related to mass transport.

As best seen in Figure 14, an alternate embodiment of the partially constricted pipette tip has an elongated constricted middle portion 14b extending between the upper and lower tip portions 14c and 14a. The elongated middle portion 14b is adapted for use with a sensor having an elongated sensing area 28, so substantially all of the sensing area is positioned within the constricted middle portion when in the sensor-extended position. In this alternate embodiment, the lower tip portion 14a is also removably connected to the middle portion 14b. The lower tip portion 14a is preferably

attached to the middle portion 14b by a friction fit therebetween, such that the lower portion can be removed and replaced during selected procedures.

As best seen in Figures 15 and 16, another alternate embodiment of the pipette tip 14 includes upper and lower tip portions 14d and 14e. The upper tip portion 14d removably attaches to the pipette's drawing tube 16, and the lower tip portion 14e is removably attached to the upper tip portion. The lower tip portion 14e of the illustrated embodiment is an elongated portion defining a micro-pipette tip that is adapted to retain samples in very low volumes ranging from 2 to 20 microliters (*i.e.*, 2-20 µl), inclusive. In the alternate embodiment as shown in Figure 16, the lower tip portion 14e defines a micropipette tip that is shorter than the lower tip portion shown in Figure 15a, and is also sized to sample the low volumes ranging from 2-20 µl, inclusive. The different lower tip portions 14d and 14e are selected for use with samples of different viscosities so as to achieve optimum performance during a sampling procedure. For example, the longer lower tip portion 14e is used with low viscosity fluids to achieve the benefit of the capillary effect within the elongated tip portion. The shorter tip portion 14e is usable with samples having higher viscosity.

As best seen in Figures 17-19, an alternate embodiment includes a pipette tip 414 that provides a tip configuration adapted to move the probe's sensor area 28 laterally within the pipette tip when in the sensor-extended position and when the sample is oscillated axially within the pipette tip. The pipette tip 414 of this alternate embodiment has a generally oval cross-sectional shape with an interior area 320 having a generally elongated "S" or "Z" shape. The interior area 320 is defined by a lower shoulder portion 322 of the pipette tip 414 that is laterally and axially offset from an upper shoulder portion 324. The lower shoulder portion 322 extends upwardly from the pipette tip's lower end and terminates at an upper surface 326 located at the interior area's mid-portion 330. The upper shoulder portion 324 is spaced upwardly apart and laterally offset from the lower shoulder portion 322 so the upper and lower shoulder portions are on opposite sides of the pipette tip's longitudinal axis. The upper shoulder portion 324 has a lower deflecting surface 332 that is angled to deflect the sample flow laterally as the sample is oscillated within the pipette tip 414.

When the pipette tip 414 is on the drawing tube 16 and before sample is drawn into the pipette tip, the sensor area 28 is in a first lateral position in the pipette tip's interior area and is substantially coaxially aligned with the pipette tip's longitudinal axis, as shown in Figure 18. When sample is drawn into the pipette tip 414, the sample flow moves upwardly through the pipette tip adjacent to the lower shoulder portion 322, and to the upper shoulder portion's deflecting surface 332. The deflecting surface 332 deflects the sample flow laterally and into the pipette tip's upper portion. This lateral movement of the sample moves the probe's sensor area 28 laterally within the pipette tip to a second lateral position, shown in Figure 17, and shown in Figure 19 in phantom lines. In this second lateral position the sensor area 28 is off-set from the pipette tip's longitudinal axis and is immediately above the lower shoulder portion's upper surface 326. As the sample is oscillated in the pipette tip 14, the sample moves along the interior area's "S" or "Z"-shaped path, thereby waggling the probe's sensor area 28 laterally in the direction of arrows F1 (Figure 17) and F2 (Figure 18) between the first and second lateral positions. The probe's lateral movement in conjunction with the oscillatory, axial sample movement provides increased relative movement between the probe's sensing area 28 and the sample, thereby minimizing mass transport problems during a sampling and testing process.

In the embodiment illustrated in Figures 1, 8, and 9, the coupling member 26 is optically coupled to a remote fiber optic spectrograph 24 (Figure 1) by the fiber optic cable 22. In an alternate embodiment of the present invention shown in Figure 15, the hand-held pipette 12 has an internal detection and analyzing device 207 such as a fiber optic spectrograph contained within a housing portion 202 attached to the pipette's handle 100. The housing portion 202 also contains a light or electromagnetic radiation source 204, a self-contained power source 206 such as a battery, and a microprocessor 205, coupled to the power source. A wave guide cable 208 optically couples the electromagnetic radiation source 204 and the detection and analyzing device 207 to the coupling member 26 of the wave-guide sensor assembly 10. The wave guide cable 208 has a sufficient length that allows the coupling member 26 to move between the sensor-retracted position and the sensor-extended position. The connecting portion 202 is adapted for receiving a portion of the wave guide cable 208 therethrough when the

coupling member is in the sensor and retracted position. Accordingly, this self-contained, hand-held pipette 12 and internal fiber optic spectrograph 200 can be carried to remote locations without concern for connection to remotely located fiber optic spectrographs, detection and analyzing devices and power sources.

In another alternate embodiment illustrated in Figure 20, a display module 210 is mounted to the pipette handle 100 and operatively coupled to the fiber optic spectrograph. The display module 210 is adapted to receive sampling results from the fiber optic spectrograph and to display the results at a location that allows a user to read the sampling results during or immediately after the sampling procedure. In one alternate embodiment, the display module is a digital display operatively coupled to the detection device 207 of the internal fiber optic spectrograph 200 on the hand-held pipette.

In an alternate embodiment of the invention shown in Figure 21, the pipette 12 includes a regulator 360 positioned in the pipette handle's bottom portion 102 and within the suction aperture 124. The regulator 360 is adapted to control the amplitude of the sample oscillation in the pipette tip by controlling the amount of air or other gas that is moved within the pipette tip 14 during the suction and pressure phases.

The regulator 360 of the exemplary embodiment is positioned in the suction aperture 124 between the air passageway 305 of the tube connector 304 and the connecting channel 136. The regulator 360 includes an upper stop 362, a lower stop 364 spaced apart from the upper stop, and a piston 366 slidably retained in the suction aperture 124 between the upper and lower stops. The piston 366 slides between the upper and lower stops 362 and 364 during the pressure and suction phases. During the pressure phase, a positive pressure is transmitted through the tube connector 304 into the suction aperture 124 above the piston 366. This positive pressure pushes the piston downwardly in the suction aperture 124 to the lower stop 364. Accordingly, the piston 366 causes movement of a selected volume of air or other gas within the connecting channel 136, the drawing tube's interior channel 110, and the pipette tip 14, thereby moving the sample to the lower position.

During the suction phase, a negative pressure is generated in the suction aperture 124 above the piston 366, and the piston is drawn upwardly from the lower

stop 364 to the upper stop 362. Accordingly, the piston 366 movement causes a selected volume of air or other gas to be drawn from the pipette tip above the sample, thereby drawing the sample within the pipette tip 14 upwardly toward the drawing tube 16.

In the exemplary embodiment shown in Figure 21, the lower stop 364 is axially adjustable to increase or decrease the piston's stroke length. The lower stop 364 is connected to an actuator rod 367 that extends through an aperture in the pipette handle's bottom portion 102. The actuator rod 367 is connected to an adjustable stop driver 368 that is adapted to selectively move the actuator rod axially, thereby moving the lower stop 364 to a selected position. The position of the lower stop 364 in the suction aperture 124 is selected to control the amplitude of the sample's oscillation in the pipette tip 14. In one alternate embodiment, the lower stop's position is initially selected to control the amount of the sample initially drawn into the pipette tip 14. The lower stop 364 is then adjusted to shorten the piston's stroke length so as to provide the desired sample oscillation during a sampling procedure without ejecting all of the sample from the pipette tip. Accordingly, the regulator 360 is adjustable to control the sample volume and the sample's oscillation amplitude in the pipette tip 14.

As best seen in Figure 22, the lower stop 364 in another alternate embodiment is connected to a rack and pinion positioning assembly 380. The positioning assembly 380 controls the lower stop's axial position within the suction aperture 124. The positioning assembly 380 includes an actuator 382 that extends through an aperture in the pipette handle's bottom portion 102. The actuator rod 382 has a distal portion with a plurality of teeth 384 thereon that defines a rack 385. The rack 385 is connected to a pinion 386 of a stop positioner 388, which is mounted to the pipette handle's bottom portion 102. The stop positioner 388 rotates the pinion 386 on the rack 385, thereby axially moving the actuator rod and the lower stop 364 to a selected position in the suction aperture 124.

In the exemplary embodiment illustrated in Figure 22, the piston 366 is biased toward the upper stop 362 by a spring 390 or other biasing member positioned in the suction aperture 124. The illustrated spring 390 is a coil spring, and the lower stop 364 is positioned within the coil spring. As the piston 366 is moved axially toward the

lower stop 364, the piston compresses the spring 390 until the piston reaches the lower stop. The spring 390 then returns the piston to a position adjacent to the upper stop 362, wherein the piston is ready for the next piston stroke.

As best seen in Figure 23, an alternate embodiment of the present invention includes a bellows regulator 370 that is operatively connected to the pneumatic tube and positioned partially within the suction aperture 124. The bellows regulator 370 is connected to a distal end portion 372 of the rod 122, which is axially movable in the suction aperture 124. The rod's distal end portion 372 has an air channel 374 therein that is connected to the pneumatic tube 302, so air or other selected gas from the tube is carried to the rod's distal end portion.

The bellows regulator 370 has an expandable bellows 376 connected to the rod's distal end portion 372 and positioned in the suction aperture 124. The bellows 376 axially expands and contracts in the suction aperture 124 during the pressure and suction phases so as to cause the sample oscillation in the pipette tip 14. The length of the bellow's axial expansion and contraction is controlled by the volume of air or other gas, or suitable liquid, moved through the hydraulic or pneumatic tube 302 during the pressure and suction phases. Accordingly, the length of axial expansion and contraction controls the positive and negative pressure generated in the pipette tip 14, thereby controlling the amplitude of the sample oscillation.

The embodiments of the present invention discussed above have been discussed primarily in connection with the use of a fiber optic probe. Alternate embodiments, however, include other sensors, such as electrochemical sensors, surface acoustic sensors, transmission absorption sensors, or the like. An alternate embodiment of the present invention, illustrated in Figure 25, has an electrochemical sensor 400 connected to the coupling member's sensor receiving member. The sensor's distal end includes an electronic conductor 402 and a pair of electrodes 404 adjacent to the conductor. The sensor's distal end is adapted to extend into the pipette tip 14 during the sample oscillation as discussed above.

The sensor's proximal end has a connector 406 that is operatively connected to an electronic cable 408. The electronic cable 408 is connected at one end to the sensor carrier 18 so as to retain the cable in a substantially fixed position relative

to the sensor 400 when the sensor is installed. The cable's opposite end (not shown) is coupled to a selected analyzer or other testing device for testing of the sample.

As best seen in Figures 22 and 24, an alternate embodiment of the invention includes a quick release sensor assembly 420 adapted to be releasably connected to the sensor carrier 18. The sensor assembly 420 includes an elongated housing 422 that contains the sensor 56. The proximal end of the housing 422 has a connection portion 424 that is received and releasably retained by the sensor carrier 18 so as to operatively connect the sensor 56 to the cable. In one embodiment, the sensor 56 is a fiber optic sensor, and the connection 402 is shaped and sized to axially align and optically couple the sensor to the fiber optic cable 22.

The connection portion 424 of the illustrated embodiment has an annular receiving area 426 that receives retaining pins 428 (Figure 22) in the lower body portion 102 of the pipette or other sampling device. The retaining pins 428 are movable between an engaged position with the pins being within the annular receiving area 426 and a released position, shown in phantom lines, with the pins being exterior of the annular receiving area. In the engaged position, the sensor assembly 420 is securely retained in the sensor carrier 18. In the released position, the sensor assembly 420 may be removed from or installed into the sensor carrier 18, and the pins are then moved to the engaged position.

The distal end portion of the housing 422 contains the sensor's sensing area 28. The sensing area 28 is space apart from housing by a space defining a flow channel 430 around the sensing area. The distal end of housing 422 is open so sample can flow into the flow channel 430. The housing 422 also includes apertures 432 at the top of the flow channel 430 that allow the sample to flow into and out of the flow channel, particularly during sample oscillation. As best seen in Figure 22, the housing's open distal end is adapted to engage and sealably engage the pipette tip 14 when installed so sample drawn into the pipette tip flows into the housing's flow channel 430 around the sensing area 28 and out of the apertures 432. Accordingly, the sensing area 28 is protected by the housing 422 while being exposed to the sample flow during the sampling procedure.

The sensor assembly 420 is particularly well suited for use with automated testing equipment. As an example, one embodiment of the invention includes an automated process of inserting the sensor assembly 420 into a pipette or other suitable sampling device when the retaining pins are in the released position, and then moving the retaining pins to the engaged position. A pipette tip 14 is then installed on the pipette's drawing tube 16 and the pipette and pipette tip are moved as a unit to a sample position wherein a selected sample is drawn into and oscillated within the pipette tip for analyzing the sample. After the sample is analyzed, it is ejected from the pipette tip, the pipette tip is ejected and the sensor assembly 420 is prepared for analyzing another selected sample. In the automated embodiment, a plurality of pipettes and sensor assemblies 420 can be used to simultaneously test or analyze a plurality of samples.

As best seen in Figure 26, another alternate embodiment of the present invention includes the wave-guide sensor assembly 10 mounted on a stand 220 used during testing of selected samples. The stand 220 has a connecting arm 222 that removably receives the wave-guide sensor assembly 10, and the connecting arm is movably mounted to a shaft 224 projecting upwardly from a base 226. The connecting arm 222 is movable with the wave-guide sensor assembly 10 relative to the base 226 between a lowered, sensing position and a raised, ready position.

The connecting arm 200 is attached to a tubular support member 228, which securely holds the coupling member 26 at a fixed location relative to the connecting arm. The probe cover 32 is concentrically mounted around the tubular support 228 and is axially movable relative to the coupling member 26 and the sensor 20 mounted thereto between a raised, sensor-exposed position to expose the sensor's sensing area 28, and a lowered, sensor position to cover and protect the sensor 20.

During a sampling procedure, the probe cover 32 is maintained in the lowered sensor-retracted position with the sensor 20 fully contained until a selected sample is ready to receive the probe's sensing area 28. The probe cover 32 is slid upwardly to the raised, sensor-exposed position, thereby exposing the sensing area 28. The wave-guide sensor assembly 10 and the stand's support arm 222 are moved downwardly as a unit relative to the stand's base 226 and the probe's sensing area 28 is

dipped into the selected sample. After completion of the sampling, the support arm 222 and wave-guide sensor assembly 10 are moved upwardly to a raised position, and the probe cover 32 is moved over the sensor 20 to the lowered, sensor-retracted position.

As best seen in Figure 27, an alternate embodiment of the invention includes a sensor assembly 450 mounted on an adjustable stand 452 that is moveable along the X, Y, and Z axes. The sensor assembly 450 includes a sensor carrier 454 mounted to an arm 456 of the stand 452. The sensor carrier 454 includes a probe cover 458 that slidably retains a sensor coupling member 460, similar to the sensor assembly discussed above in connection with the pipette. The coupling member 460 is attached to the fiber optic cable 22 and is adapted to removably receive the sensor 56 therein.

As best seen in Figure 28, the sensor carrier's bottom portion 462 is attached to a base assembly 464 that is substantially similar to bottom portion of the pipette handle discussed above. A tip ejector 150 is attached to the bottom portion 462 for ejection of the pipette tip 14 from the drawing tube 16. The bottom portion 462 also includes a sensor receiving aperture 108 that is coaxially aligned with the drawing tube 16. An air passageway 466 extends through the bottom portion 462 and communicates with the receiving aperture 108 and the drawing tube's interior area 110. A pneumatic tube 470 is connected to the other end of the air passageway 466 so air or other gas can be used to create positive and negative pressures in the pipette tip 14 for oscillation of the sample therein, as discussed above. In the illustrated embodiment, the tube 470 is removable connected to the bottom portion 462 and an O-ring seal 472 is positioned between the tube and the bottom portion to maintain a substantially air-tight seal therebetween.

In an another alternate embodiment of the invention shown in Figure 29, a plurality of the stand-mounted sensor assemblies 450 are mounted to a support structure 474, such as a stand assembly of an automated sampling device. The plurality of sensor assemblies 450 retain the sensors 56 therein. The support structure 474 includes a plurality of drawing tubes 16 that are positioned to removably receive pipette tips 14 thereon in a position to receive the sensors 56 when the sensors are in the sensor-extended position, as discussed above. Accordingly, the plurality of sensor assemblies 450 are usable simultaneously to test or analyze a plurality of samples.

Referring to Figures 30A-F, an alternate embodiment of the pipette 12 is illustrated. This alternate embodiment is similar to the pipette discussed above, and it has an elongated handle 100, an ergonomically-shaped thumb-activated plunger 114 and a retaining hook 115 adjacent to the plunger. The retaining hook 115 allows the pipette 12 to be hung on a retaining stand, or the like, such as during a long sampling procedure or when the pipette is not being used.

Experimental Examples

In order to better demonstrate the advantages of the present invention, several experiments were conducted. The results of these experiments are shown in Figure 31 and Figures 32A-C. The materials employed in these experiments included a Biacore probe instrument apparatus for surface plasmon resonance (SPR) detection, Sensor Probes CM5 for SPR, HBS buffer as a reference solution, and an amine coupling kit containing NHS, EDC, and ethanolamine (commercially available products from Biacore AB, Uppsala, Sweden), as well as sodium hydroxide TITRISOL (commercially available from Merck, Darmstadt, Germany). In addition, a prototype of the present invention, amino-H1 hapten, and monoclonal antibody were internally produced for purposes of experimentation.

Initially, a high-capacity ligand sensor surface was prepared by coupling a small molecule, amino-H1 hapten, to the carboxy methylated dextrane on the sensor probe. The carboxy-groups of the carboxy methylated dextrane were activated by a mixture of N-ethyl-N'-(dimethyl-aminopropyl) carbodiimide hydrochloride (EDC), and N-hydroxysuccinimide (NHS), both prepared in water. A solution of an amino derivative of a small molecule, hapten H1, was coupled to the activated groups on the sensor surface. Residual NHS-esters remaining after the ligand immobilization were then reacted with a solution of ethanolamine. Each of the three steps in this immobilization took 15 minutes and were performed at room temperature, 20°C.

The sample used was a monoclonal mouse antibody (Mab 515) directed against the H1 hapten. The concentration of the antibody was 1 or 0.3 μg/ml diluted in HBS buffer. The interaction time for the antibody sample with the sensor surface was three and five minutes, respectively. The sensor probe was reused a number of times by

regenerating it with 0.1 M sodium hydroxide and one minute of interaction. All of the experiments were performed at room temperature, 20°C.

The general method used in the experiments were as follows: (1) draw reference solution (HBS); (2) read measured SPR-response of reference; (3) dispense HBS; (4) aspirate sample; (5) dispense sample; (6) aspirate HBS; (7) dispense HBS; (8) aspirate HBS; (9) read measured SPR-response for sample interaction; and (10) regenerate sensor.

Referring now to Figure 31 and Figures 32A-C, experimental data is illustrated for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10 and 11. Specifically, Figure 31 compares the measured SPR-response of a non-oscillated sample, "A," with the SPR-response of an oscillated sample, "B." Here, sample Mab 515 (concentration 1 μg/ml) was manually drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. As shown, the sensor response increased approximately three-fold when the sample was oscillated.

Figures 32A-C compare the measured SPR-response of a non-oscillated sample with the SPR-response of an oscillated sample within a constricted pipette tip in accordance with the embodiment of the invention as shown in Figure 13. More specifically, Figure 32A demonstrates the influence that a sample's oscillation frequency and amplitude have on the measured SPR-response. Here, sample Mab 515 (concentration 1 μg/ml) was manually drawn into the constricted pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. As shown, the sensor response increased as the frequency and amplitude of sample oscillation was increased. In Figure 32A, "A" shows the SPR-response with no oscillation; "B" shows the SPR-response with low frequency and small amplitude of oscillation; and "C" shows the SPR-response with high frequency and small amplitude of oscillation; and "D" shows the SPR-response with high frequency and large amplitude of oscillation. These results indicate that as the frequency of oscillated forced convention is increased, the sensor response is also increased.

Figure 32B demonstrates the influence that the pipette tip (flow cell) geometry has on the measured SPR-response. Here, sample Mab 515 (concentration 1

μg/ml) was drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. In Figure 32B, "A" shows the SPR-response of an oscillated sample within a pipette tip, whereas "B" shows the SPR-response of an oscillated sample within a constricted pipette tip. These results illustrate the improved flow dynamics within the constricted tip.

Figure 32C compares the measured SPR-response of a non-oscillated sample within a Gilson pipette tip with an oscillated sample and an oscillate reference solution, both of which were within a constricted pipette tip. Here, sample Mab 515 (concentration 0.3 μg/ml) was manually drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for five minutes. In Figure 32C, "A" shows the SPR-response of a non-oscillated sample within a pipette tip; "B" shows the SPR-response of an oscillated sample within a constricted pipette; and "C" shows the SPR-response of an oscillated reference solution (HBS buffer) within a constricted pipette tip. These results also demonstrate the improved sensor response at oscillating forced sample convections.

Although specific embodiments of, and examples for, the present invention have been described above for purposes of illustration, various modifications can be made without departing from the spirit and scope of the invention, as will be evident by those skilled in the relevant art. For example, the sensor assembly 10 may be removably mounted to a tubular pipette adapter that removably receives the drawing tube of a conventional pipette and that provides an adapter drawing tube which coaxially aligns with the sensor assembly for drawing of the selected sample. Such a retrofit or adapter for a conventional pipette provides many benefits achieved by the exemplary embodiments discussed above and illustrated in the drawings. The teachings provided herein of the present invention can be applied to other sensor assemblies and other sampling devices, not necessarily those limited to hand-held, manually activated sampling devices. As an example, the pipette 12 or other sampling device can be provided with a motorized pumping mechanism adapted to create the selected partial vacuum at the drawing tube as is provided by the manual drawing mechanism described above.

Furthermore, while the present invention is generally described as being applied to pipettes and fiber optic sensors, the principles of the present invention can be

applied to other sampling devices and sensor systems. Accordingly, the invention is not limited by the disclosure, but instead its scope is to be determined entirely from the following claims.

CLAIMS

We claim:

1. A sensor assembly for use with a signal source and a signal carrying member connected to the signal source, comprising:

a sensor having a probe, the probe having a first end portion, a second alignment end portion, and a sensing area, the sensing area being a probe area at which the signal is generated or passed through; and

a sensor carrier having a receiving member attachable to the signal carrying member and attachable to the sensor, the receiving member being shaped to align the second alignment end portion of the probe with the signal carrying member for propagating a signal from the signal carrying member to the probe at the second alignment end portion.

2. The sensor assembly of claim 1 wherein the sensor is a wave-guide sensor, the probe is a wave-guide probe, the sensor carrier is a wave-guide sensor carrier, and the receiving member is a wave-guide receiving member, the wave-guide receiving member being shaped to align the second alignment end portion of the wave-guide probe with a wave-guide cable that is the signal carrying member for propagating electromagnetic radiation into the wave-guide probe.

3. The sensor assembly of claims 1 or 2, further comprising:

a pipette retaining the sensor carrier in an installed position.

4. The sensor assembly of claim 3, further including a drawing mechanism connected to the pipette and a pipette tip removably connected to the pipette and positioned to receive a portion of the probe therein, the drawing mechanism being operatively coupled to the pipette tip to generate a selected negative pressures in the pipette tip to allow a selected volume of a liquid sample to be moved within the pipette tip relative to the position of the probe.

5. The sensor assembly of claim 4 wherein the drawing mechanism is a sample handling mechanism operatively coupled to the pipette tip to generate selected positive and negative pressures in the pipette tip to allow a selected volume of a liquid sample to be moved within the pipette tip relative to the position of the probe.

6. The sensor assembly of claim 3, 4 or 5 wherein the sensor carrier is removably attached to the pipette and movable between an installed position with the sensor carrier in engagement with the pipette and a removed position with the sensor carrier being out of engagement with the pipette.

7. The sensor assembly of claim 6 wherein the pipette includes a locking mechanism releasably attached to the sensor carrier when the sensor carrier is in the installed position.

8. The sensor assembly of claim 3, 4, or 5 wherein the pipette has a a tip receiving portion coupled to the drawing mechanism, and a tip ejector connected to the drawing mechanism and positioned adjacent to the tip receiving portion, the tip receiving portion being shaped to releasably receive a pipette tip thereon and the drawing mechanism being activatable to move the tip ejector relative to the tip receiving portion between a withdrawn position and an ejection position, the tip ejector being positioned to eject a pipette tip from the tip receiving portion when the tip ejector is moved to the ejection position.

9. The sensor assembly of claim 8 wherein the sensor carrier has a probe cover attached to the receiving member, the probe cover defining an interior area sized to contain the sensing area of the probe, the receiving member being movable relative to the probe cover between a sensor exposed position and a sensor retracted position, the tip ejector being in engagement with the drawing mechanism when the probe cover is in the sensor-retracted position for ejection of the pipette tip and the tip ejector being out of engagement with the drawing mechanism when the probe cover is in the sensor-extended position to prevent ejection of the pipette tip.

10. The sensor assembly of claims 1, 2, 3, 4, or 5 further comprising a probe cover attached to the receiving member, the probe cover defining an interior area sized to contain the sensing area of the probe, the receiving member being movable with the sensor as a unit relative to the probe cover for movement of the probe between a first position with the sensing area of the probe contained in the interior area of the probe cover and a second position with the sensing area of the probe being exposed and exterior of the interior area.

11. The sensor assembly of claim 10 wherein the sensor carrier includes detents that releasably retain the probe cover in the first and second positions.

12. The sensor assembly of claim 10 wherein the receiving member is slidably connected to the probe cover for movement of the probe between the first and second positions.

13. The sensor assembly of claim 10 wherein the probe cover is a generally cylindrical tube.

14. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is removably connected to the receiving member.

15. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is a fiber optic sensor and the probe is a fiber optic probe.

16. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor has a connecting member attached to the probe, and the receiving member is attachable to the connecting member of the sensor.

17. The sensor assembly of claim 1, 2, 3, 4, or 5, further including a protective storage housing removably attachable to the sensor, the protective storage housing extending over at least a portion of the probe and containing the sensing area.

18. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is a surface plasmon resonance sensor.

19. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the receiving member is removably attachable to the signal carrying member.

20. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the receiving member is integrally connected to the signal carrying member.

21. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor includes a connecting member connected to the probe, and the receiving member is attached to the connecting member.

22. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensing area is between the first end portion and the second alignment end portion.

23. The sensor assembly of claim 3 ,4, or 5, further comprising a pipette tip removably connected to the pipette and positioned to receive the sensing area of the sensor therein, the pipette tip including a lower tip portion having a first cross-sectional area, an upper tip portion having a second cross-sectional area, and a constricted middle portion between the lower and upper tip portions, the constricted middle tip portion having a third cross-sectional area that is less than the first and second cross-sectional areas of the lower and upper tip portions.

24. The sensor assembly of claim 3, 4, or 5, further comprising a pipette tip connected to the pipette and positioned to receive the sensing area of the sensor therein, the pipette tip having a first tip portion and a second tip portion removably attached to the first portion, the first tip portion being adapted to retain sample volumes ranging from 2 to 20 microliters, inclusive.

25. The sensor assembly of claim 3, 4, or 5, further comprising a pipette tip connected to the pipette and positioned to receive the sensing area of the sensor therein, the

sensing area being movable laterally relative to the pipette tip when the sensing area is in the pipette tip, the pipette tip being adapted to allow the sensing area of the wave guide probe to waggle between a first extended position and a second axial position when the volume of a selected sample within the pipette is oscillated.

26. The sensor assembly of claim 25 wherein the pipette has first and second shoulder portions axially and laterally offset from each other to define a laterally offset interior area.

27. The sensor assembly of claim 26 wherein the interior area has a substantially Z-shaped cross-sectional area.

28. The sensor assembly of claim 3, 4, or 5 wherein the pipette has a retaining portion that engages the wave-guide-sensor carrier and releasably retains the wave guide receiving member.

29. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is a sample (bulk) solution absorbance sensor.

30. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is an electrochemical sensor and the probe is an electronic probe.

31. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is a surface acoustic wave sensor, and the probe is an electronic probe.

32. A method of analytically sampling a selected chemical sample with a sensor assembly coupled to an analyzer and a signal source, comprising the steps of:

providing a sensor carrier with a receiving member coupled to the analyzer and the signal source by a signal carrying member, the receiving member having a coupler and a sensor cover attached to the coupler;

removably attaching the sensor to the receiving member and connecting an end portion of the sensor with the signal carrying member, the sensor having a sensing area spaced apart from the end portion of the sensor;

propagating a selected signal between the signal source and the sensing area of the sensor through the signal carrying member and the sensor;

moving the sensor relative to the sensor cover from a sensor contained position with the sensing area of the sensor being covered by the sensor cover to a sensor extended position with the sensing area being exterior of the sensor cover and exposed;

contacting the selected chemical sample with the sensing area of the sensor after the sensor is attached to the receiving member and the sensor is in the sensor extended position; and

analyzing with the analyzer the signal thereto through the signal carrying member from the sensing area of the sensor when the sensing area is contacting the selected chemical sample to analytically sample the selected chemical sample.

33. The method of claim 32, further including the steps of withdrawing the sensor from the selected chemical sample and moving the sensor from the sensor extended position to the sensor contained position with the sensing area being covered by the sensor cover.

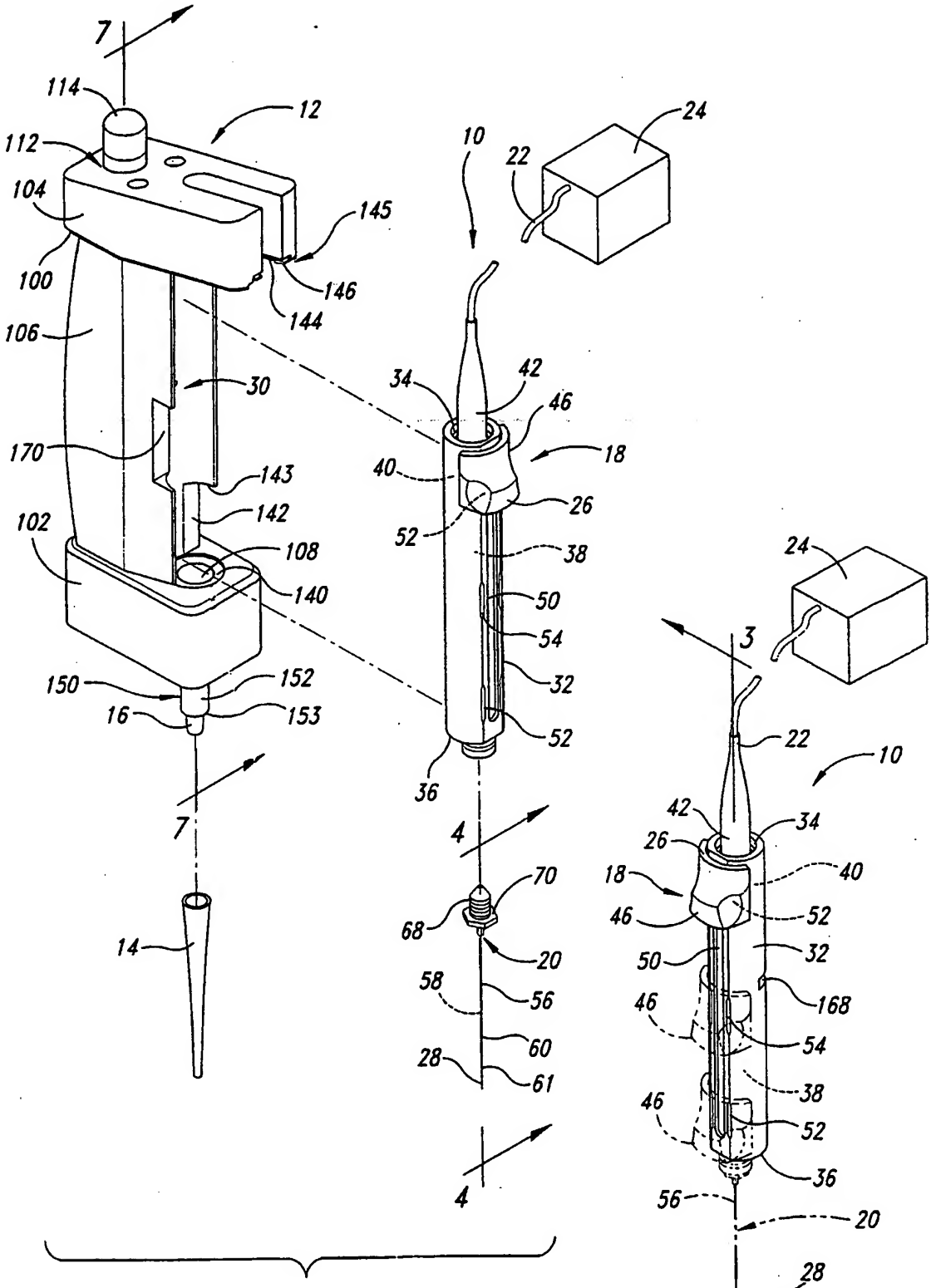
34. The method of claim 33, further including the steps of moving the sensor to the sensor extended position after the sensor has been withdrawn to the sensor contained position, and then contacting the sensing area with a second selected chemical sample when the sensor is in the sensor extended position.

35. The method of claim 34 wherein the sensor is a first sensor, and further including the steps of removing the first sensor from the receiving member after chemically analyzing the selected chemical sample, and removably attaching a second sensor to the sensor carrier.

36. The method of claim 32 wherein the step of contacting the selected chemical sample with the sensing area of the sensor includes moving the selected chemical sample into contact with the sensing area, and the step of analyzing with the analyzer occurs substantially simultaneously as the selected chemical sample is moved into contact with the sensing area of the sensor.

37. The method of claim 32, further including the step of oscillating the sample relative to the sensor when the sensing area of the sensor is in contact with the selected chemical sample.

38. The method of claim 32 or 37, further including the step of moving the sensor laterally relative to the sample when the sensing area of the sensor is in contact with the selected chemical sample.


7
114
12
112
104
145
100
146
144
106
30
170
143
142
102
108
140
150
152
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153
7
14
10
22
24
34
42
46
18
40
26
52
38
50
54
32
52
36
4
70
68
20
58
56
60
28
61
4
3
24
22
10
42
34
26
40
18
46
52
50
32
168
46
54
38
46
52
36
56
20
28
3

Fig. 1

Fig. 2

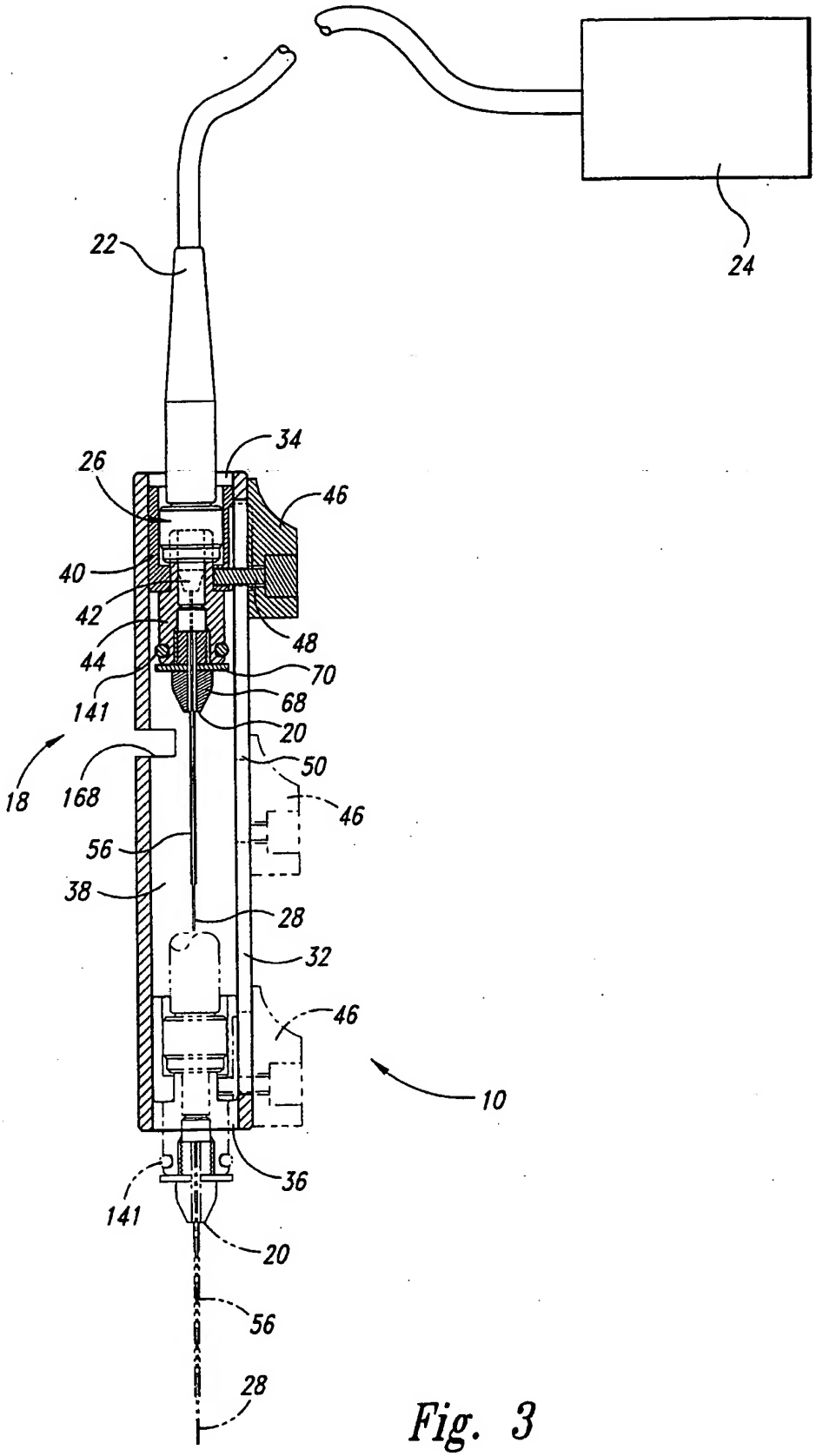

22
24
34
26
46
40
42
48
44
70
141
68
20
18
168
50
46
56
38
28
32
46
10
36
141
20
56
28

Fig. 3

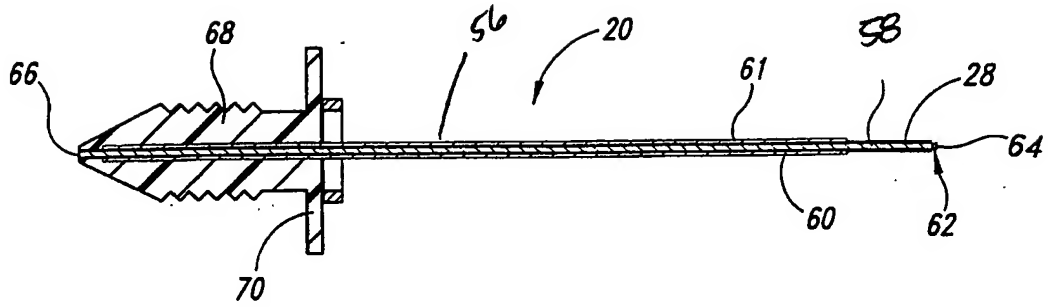


Fig. 4

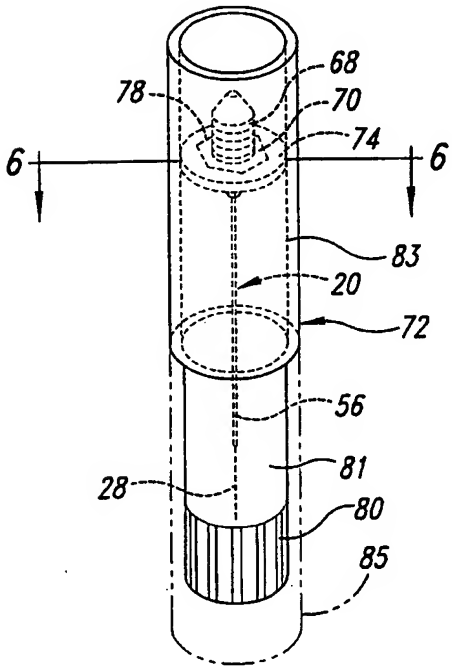


Fig. 5

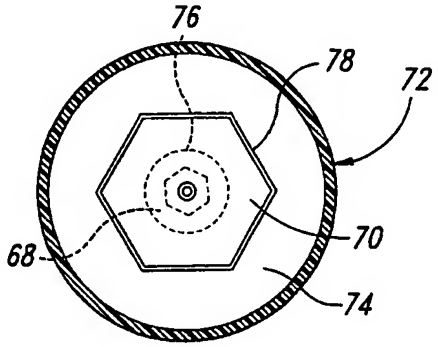
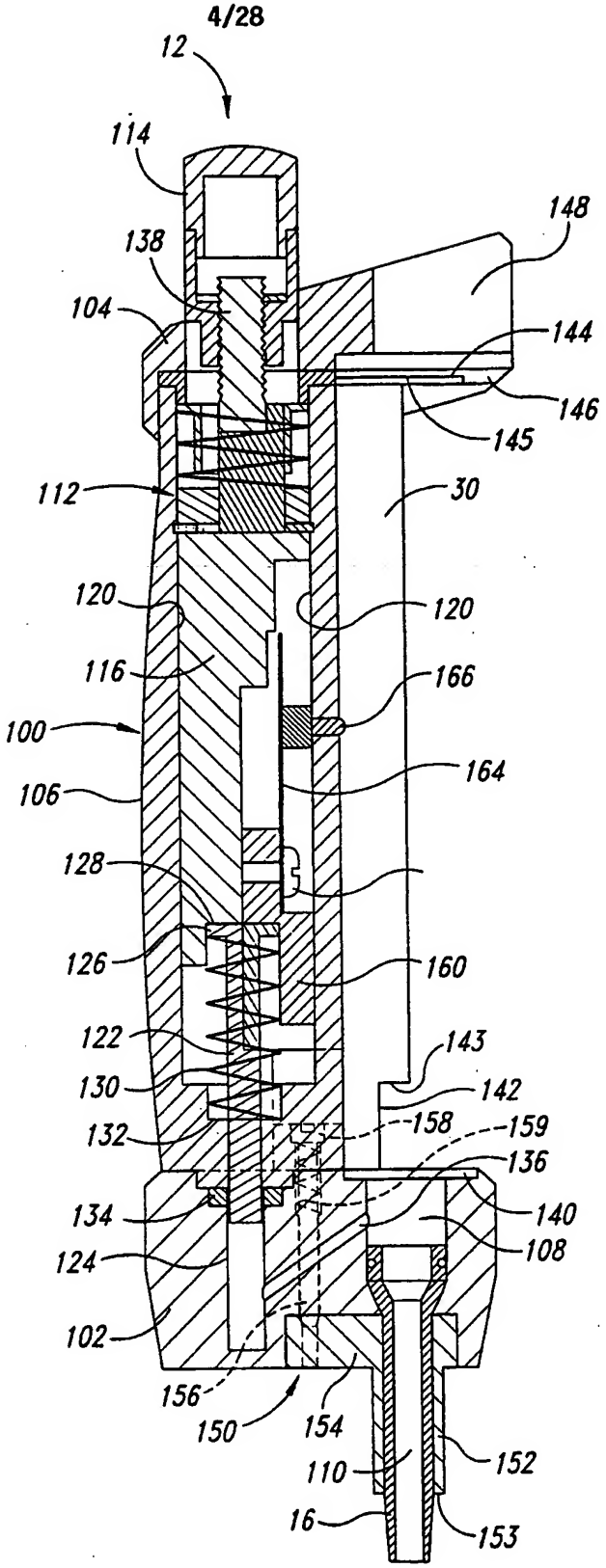


Fig. 6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114
148
138
104
144
146
145
112
30
120
120
116
166
100
164
106
128
126
160
122
143
130
142
132
158
159
136
134
140
124
108
102
156
150
154
152
110
16
153

Fig. 7

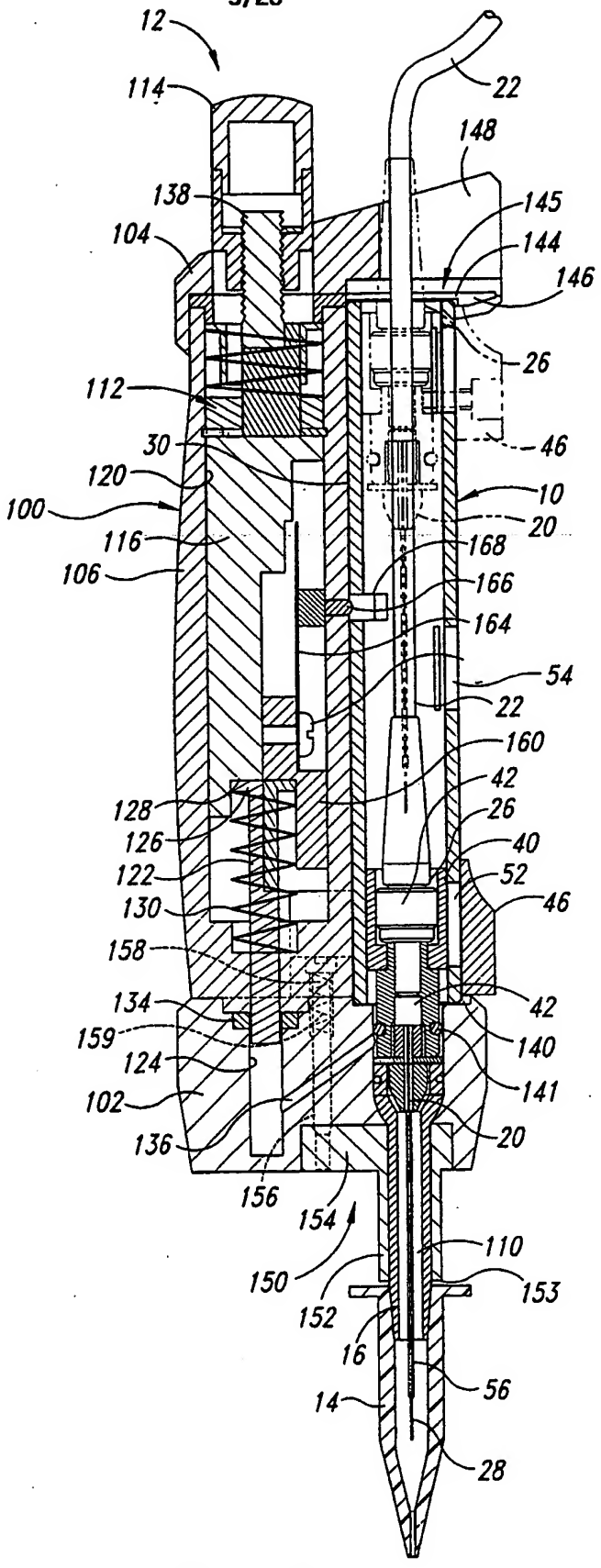
12
114
22
148
138
145
104
144
146
26
112
46
30
120
10
100
20
116
168
106
166
164
54
22
160
42
128
26
126
40
122
52
130
46
158
42
134
140
159
124
141
102
20
136
156
154
110
150
153
152
16
56
14
28

Fig. 8

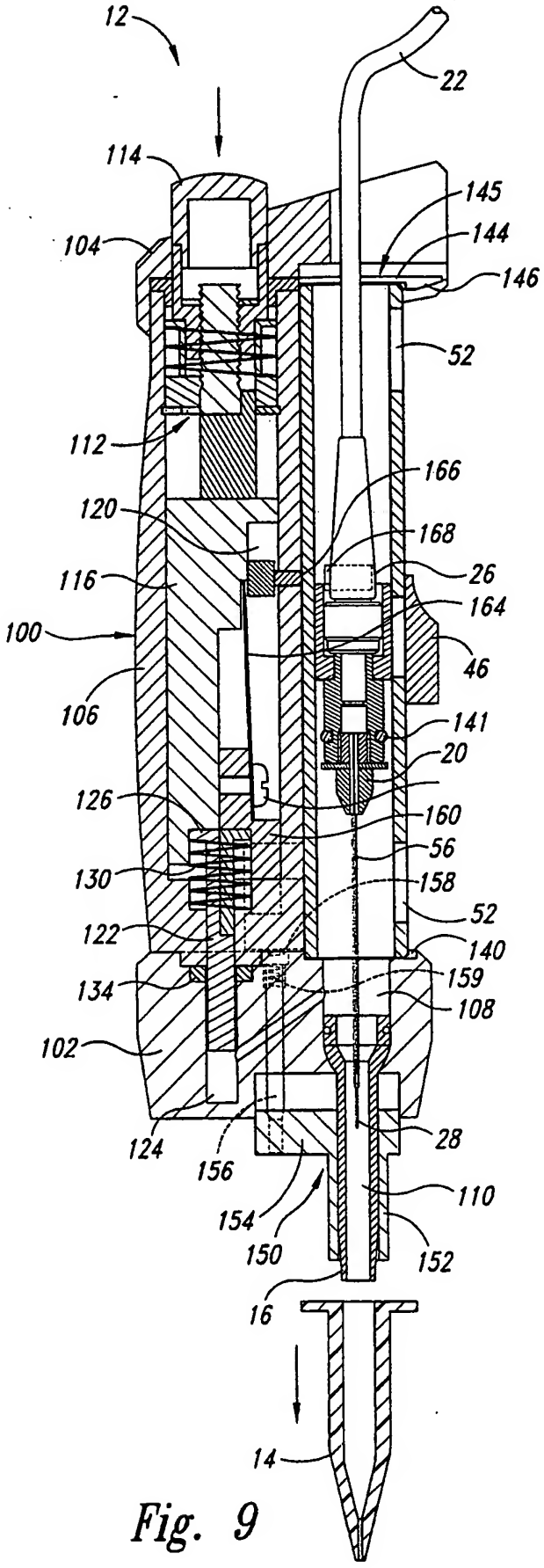
12
22
114
145
144
104
146
52
112
166
120
168
26
116
164
100
46
106
141
20
126
160
56
130
158
52
122
140
159
134
108
102
28
124
156
110
154
150
152
16
14

Fig. 9

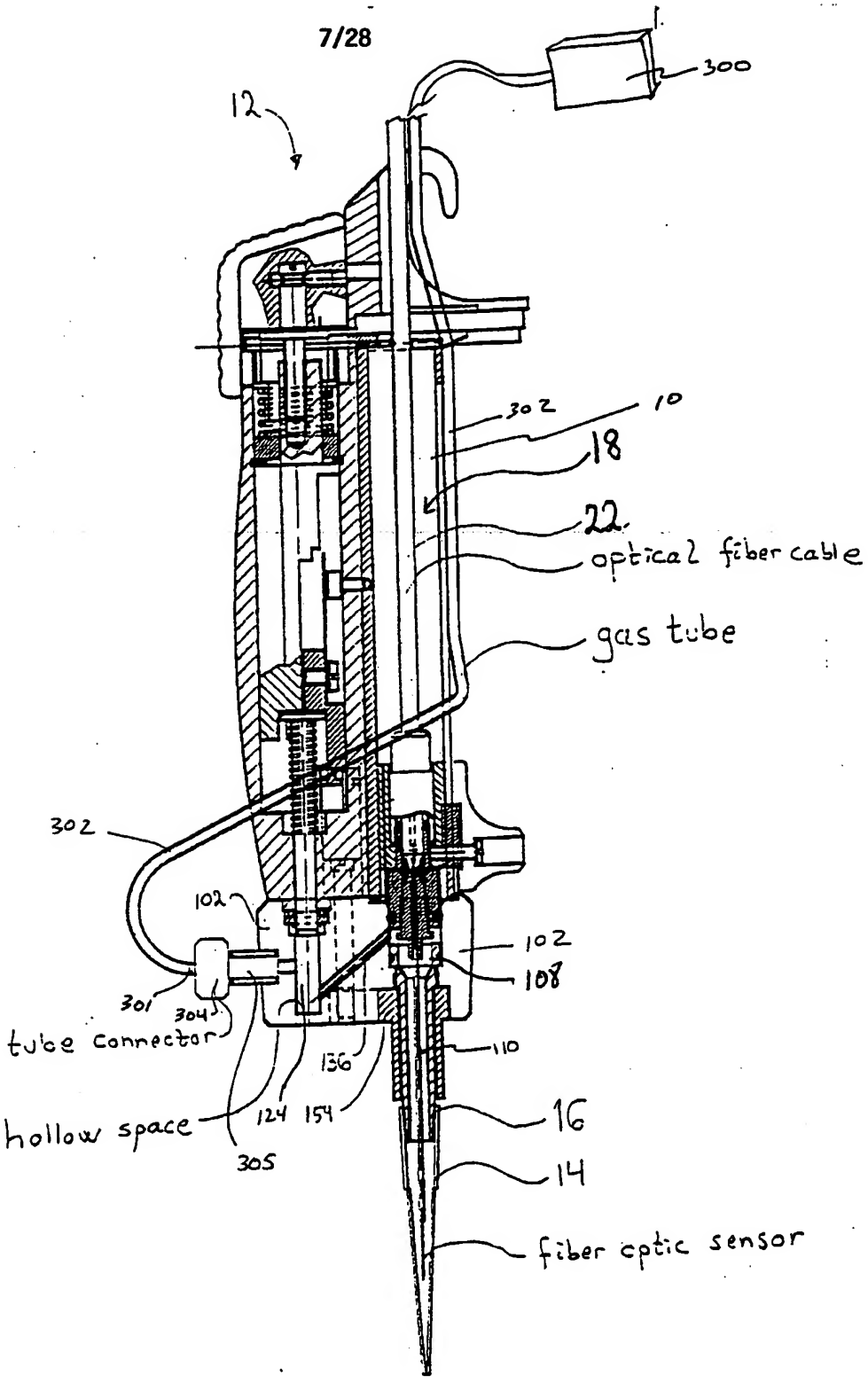
300
12
302
10
18
22
optical fiber cable
gas tube
302
102
102
108
301
304
tube connector
110
136
hollow space
124
154
16
305
14
fiber optic sensor

Figure 10

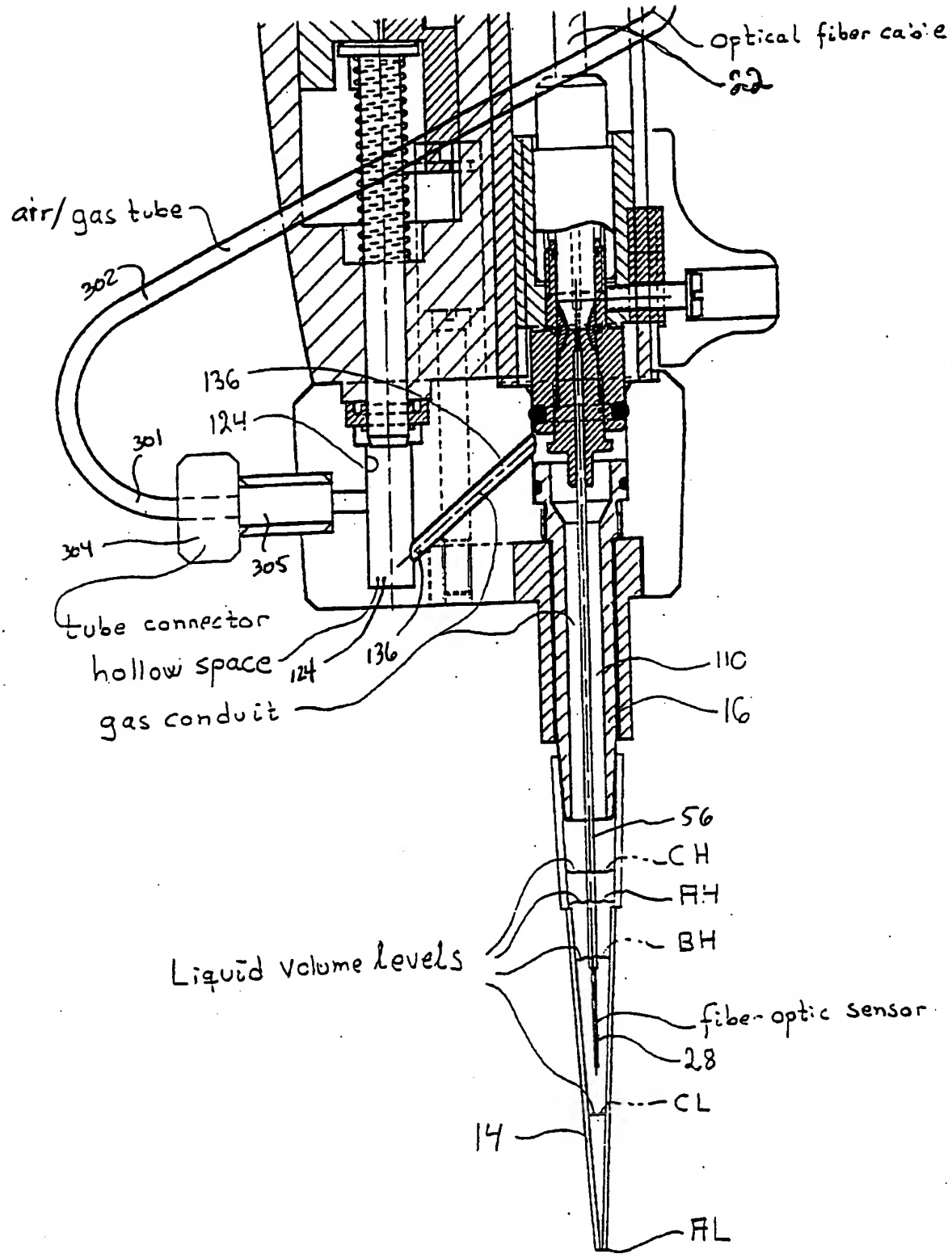
optical fiber cable
22
air/gas tube
302
136
124
301
304
305
tube connector
hollow space
124
136
gas conduit
110
16
56
CH
AH
BH
Liquid volume levels
fiber-optic sensor
28
CL
14
AL

Figure 11

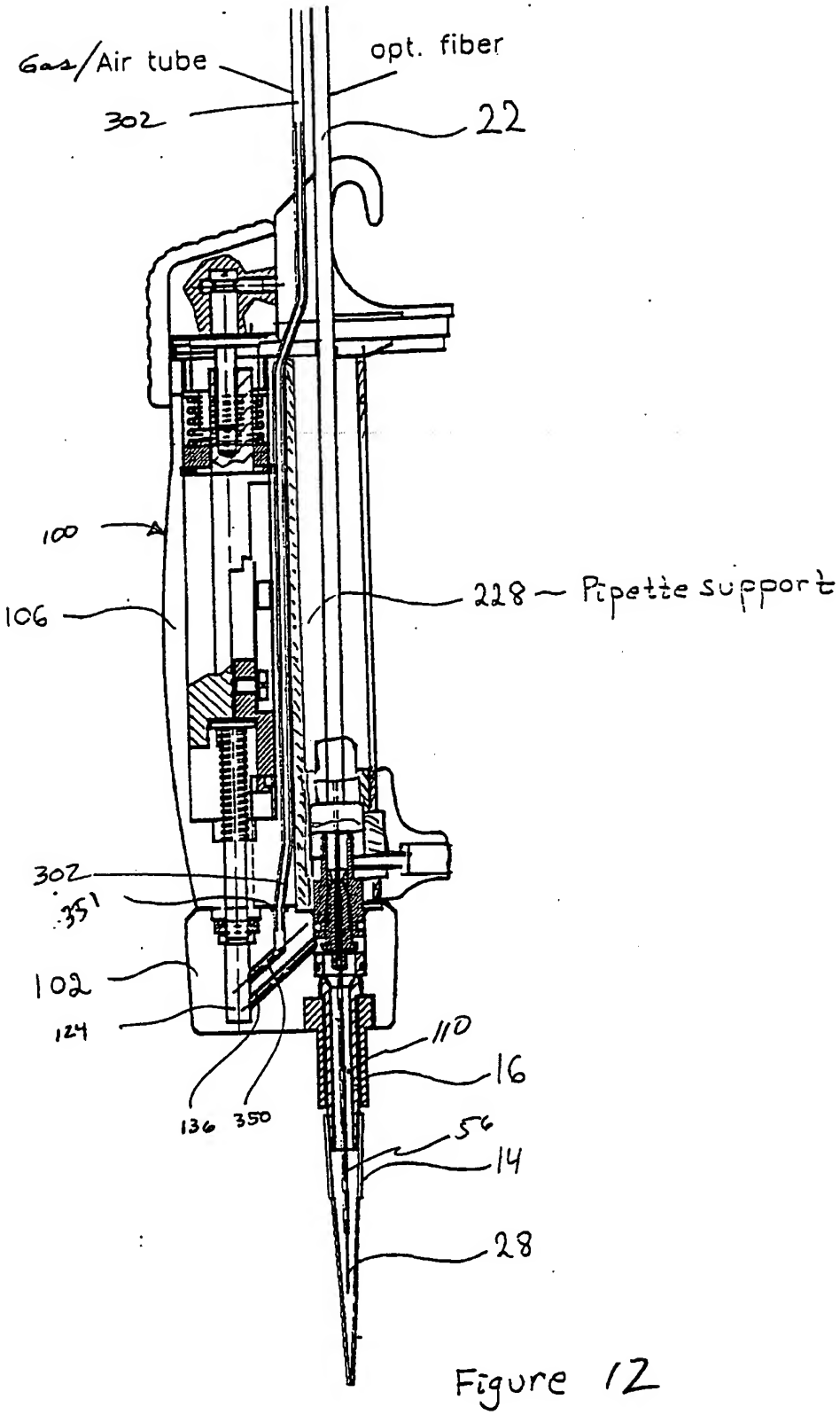
Gas/Air tube
opt. fiber
302
22
100
106
228 ~ Pipette support
302
351
102
124
110
16
136
350
56
14
28

Figure 12

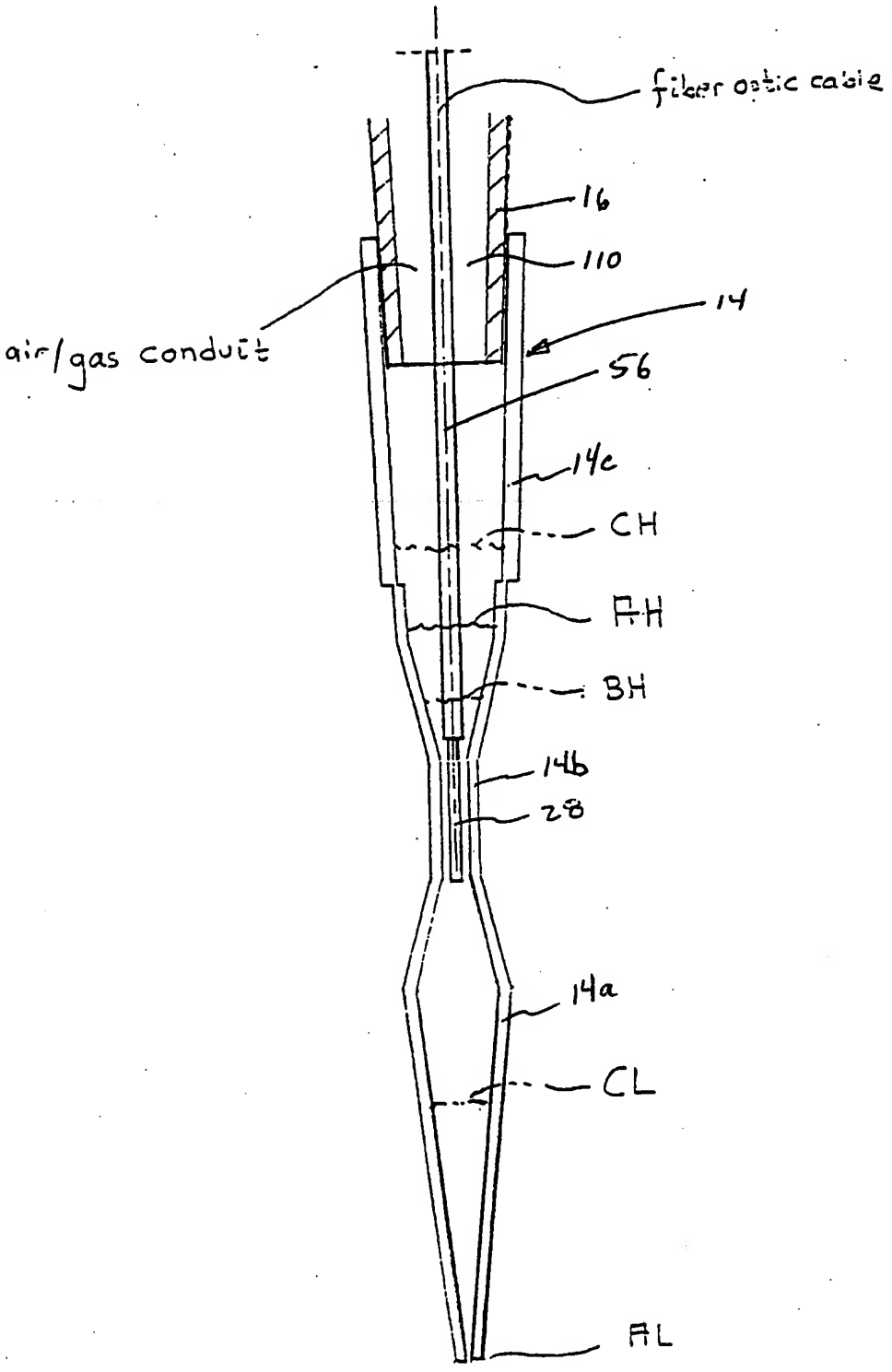
fiber optic cable
16
110
14
air/gas conduit
56
14c
CH
FH
BH
14b
28
14a
CL
AL

Figure 13

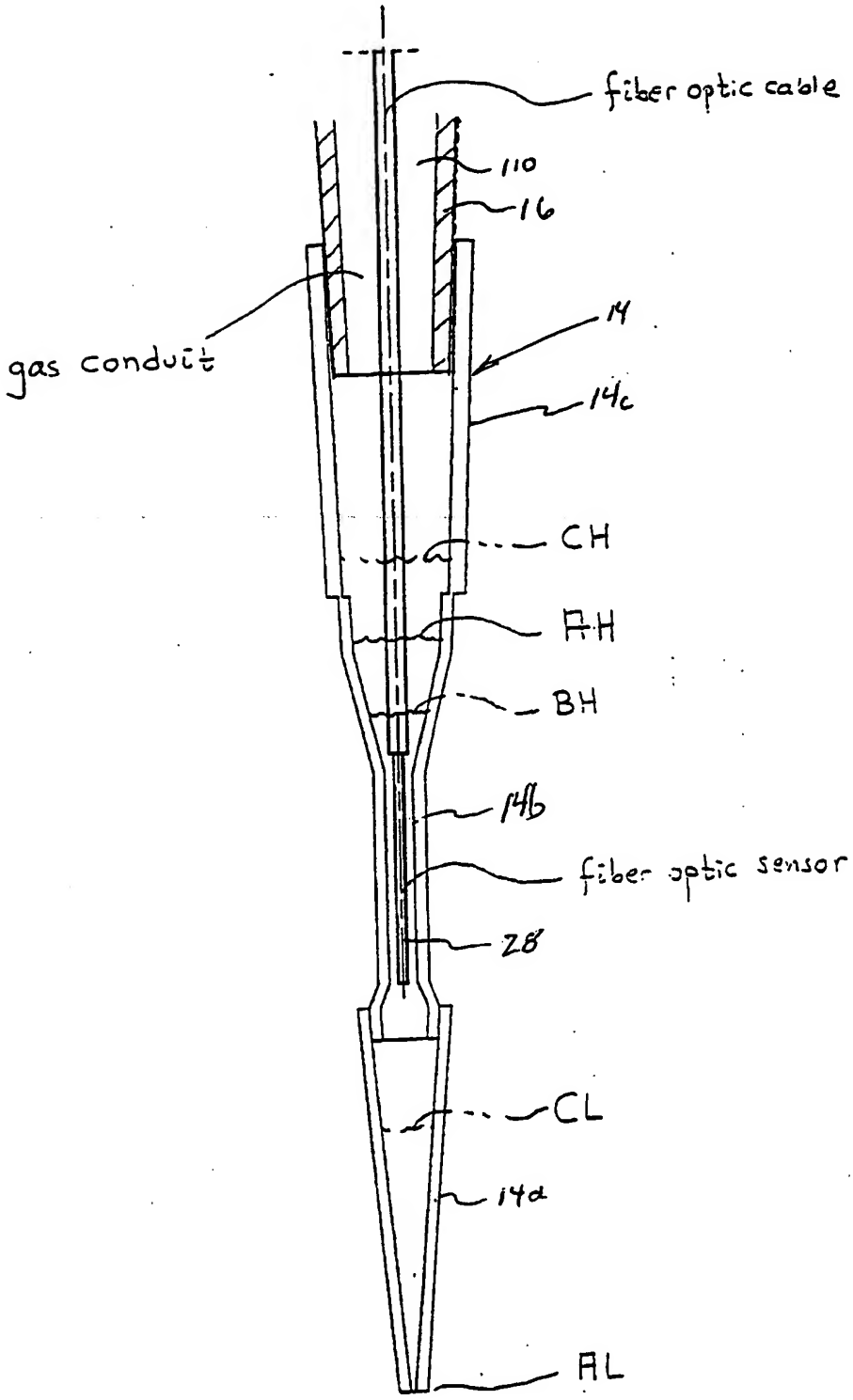
fiber optic cable
110
16
gas conduit
14
14c
CH
AH
BH
14b
fiber optic sensor
28
CL
14a
AL

Figure 14

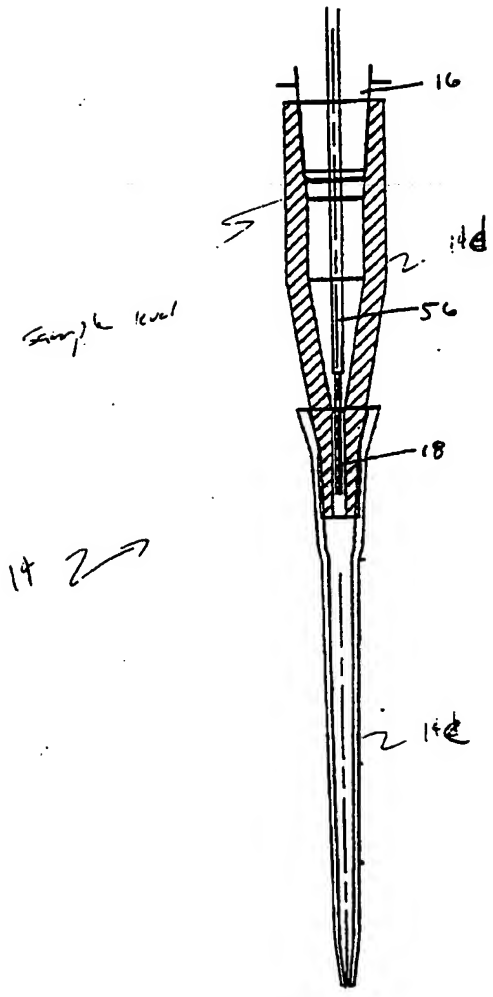

Figure 15

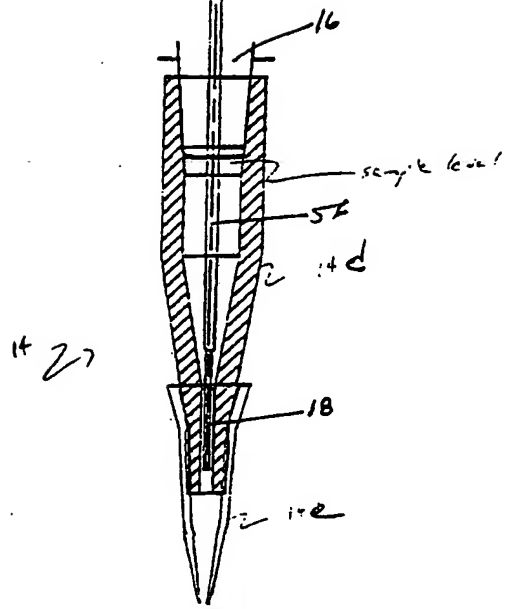

Figure 16

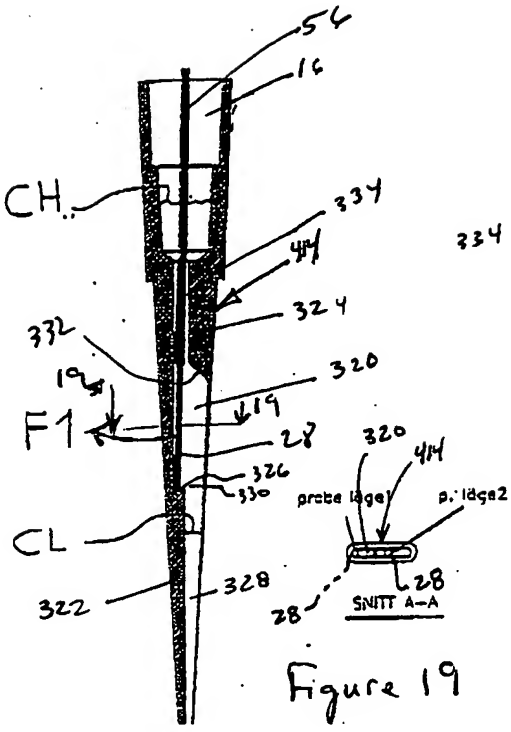

Figure 19

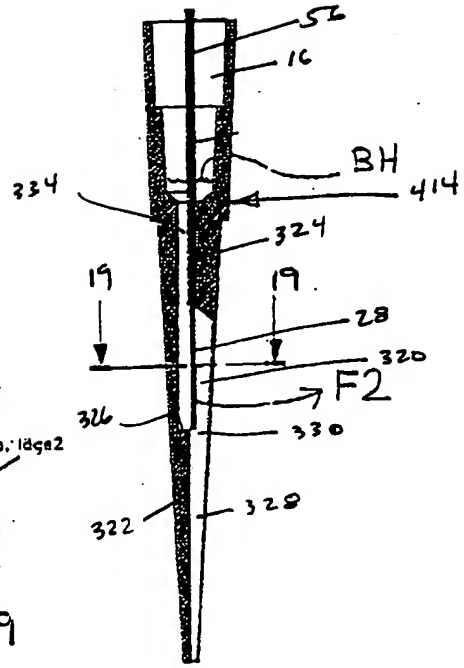

Figure 17

Figure 18

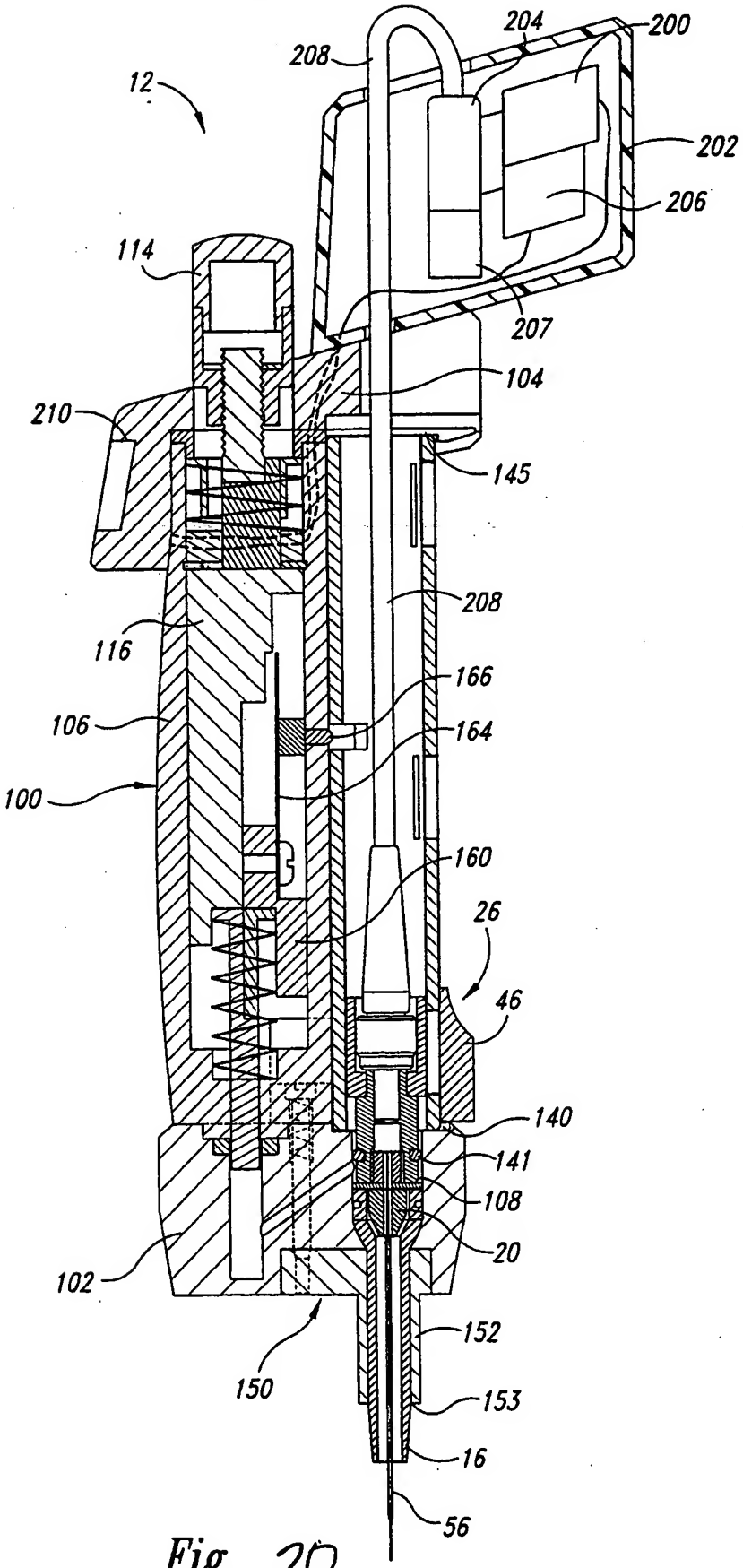
204
200
208
12
202
206
114
207
104
210
145
208
116
166
106
164
100
160
26
46
140
141
108
20
102
152
150
153
16
56

Fig. 20

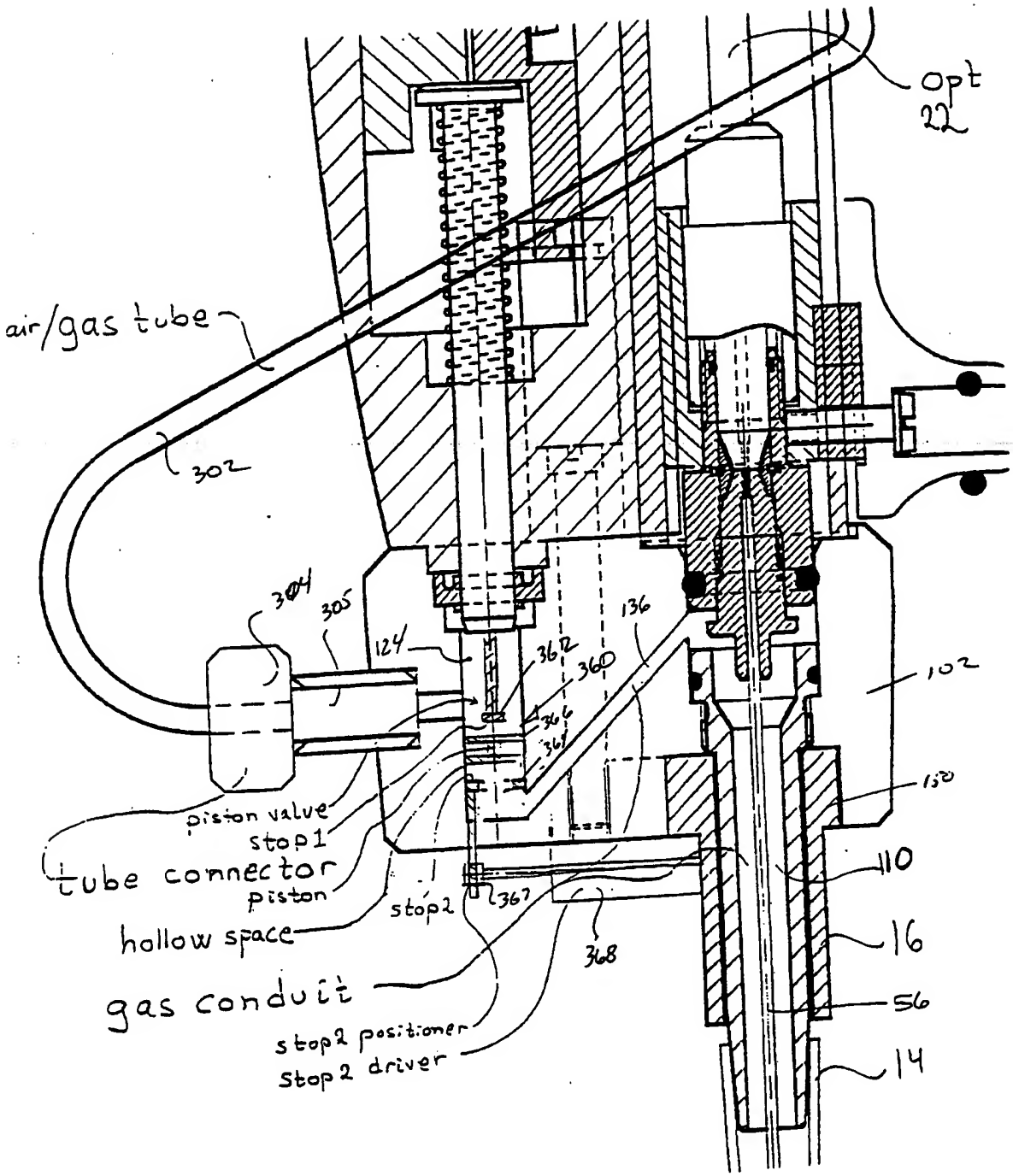
opt 22
air/gas tube
302
304
305
124
136
102
piston valve
stop1
tube connector
piston
hollow space
gas conduit
stop2
stop2 positioner
Stop2 driver
110
16
56
14

Figure 21

Probe in flow cell housing

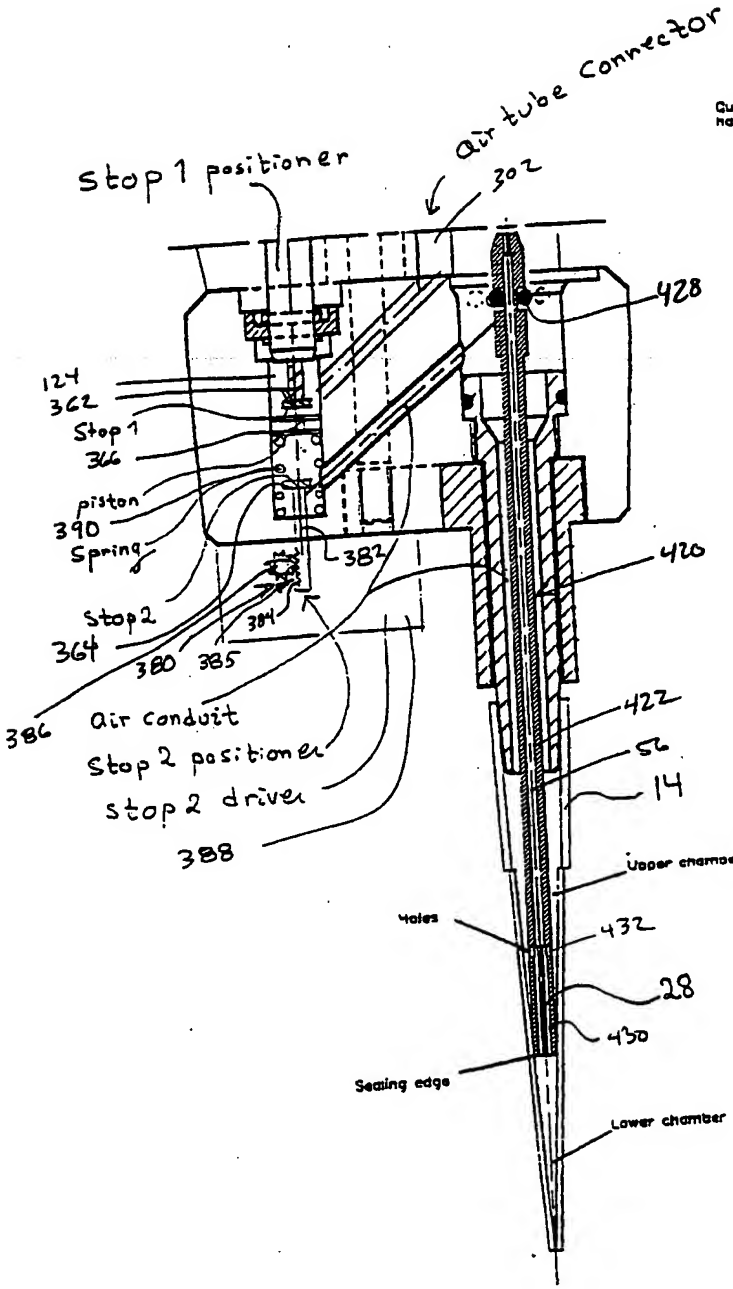

Figure 22

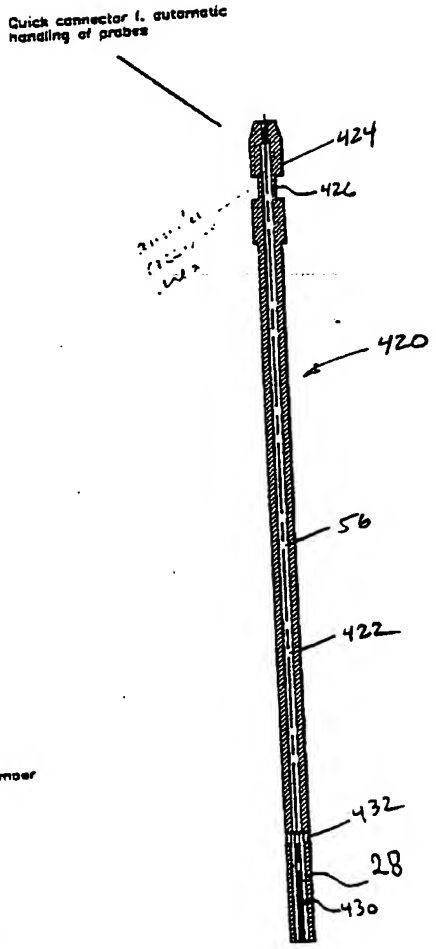

Figure 24

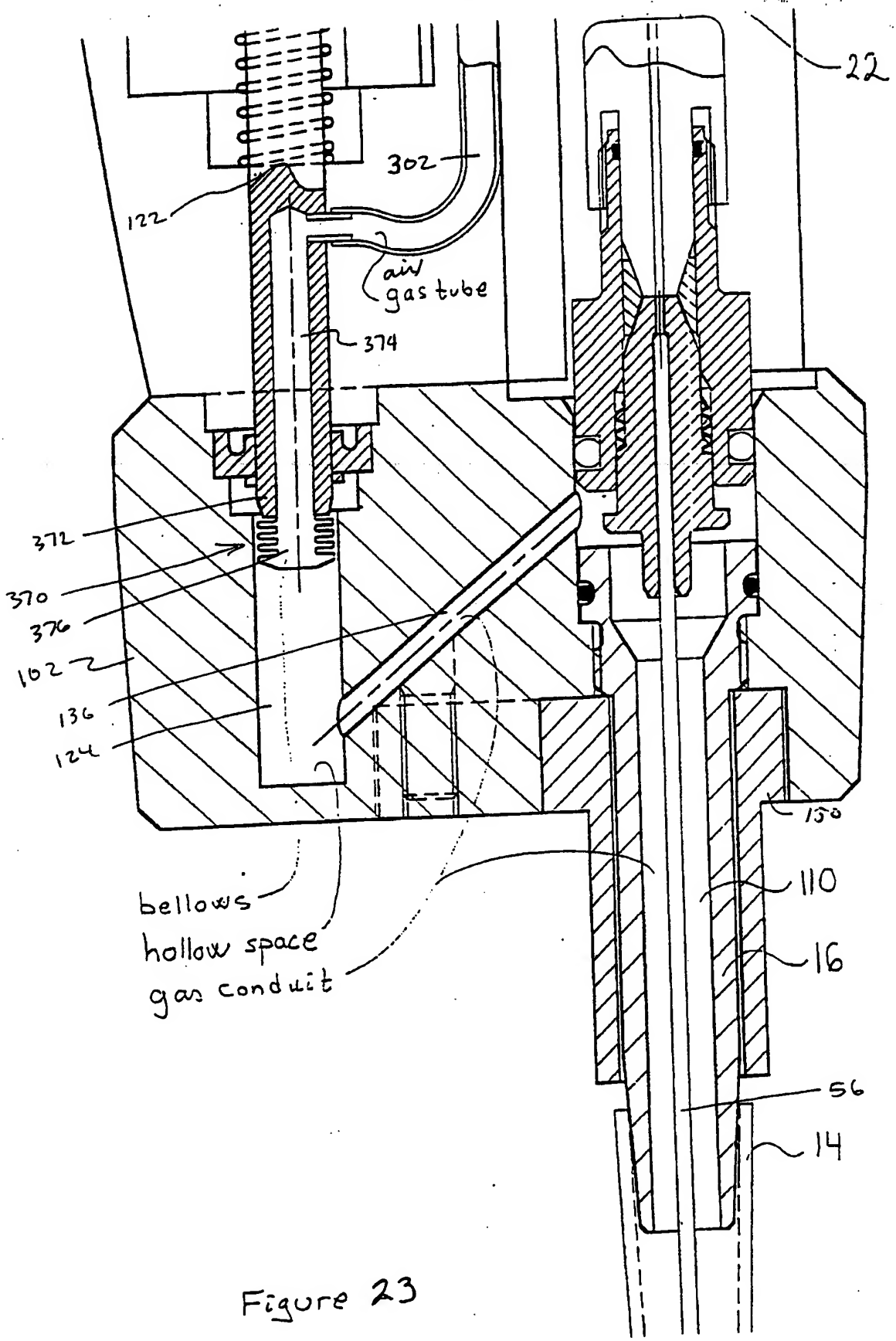
22
302
122
air gas tube
374
372
370
376
102
136
124
150
bellows
hollow space
gas conduit
110
16
56
14

Figure 23

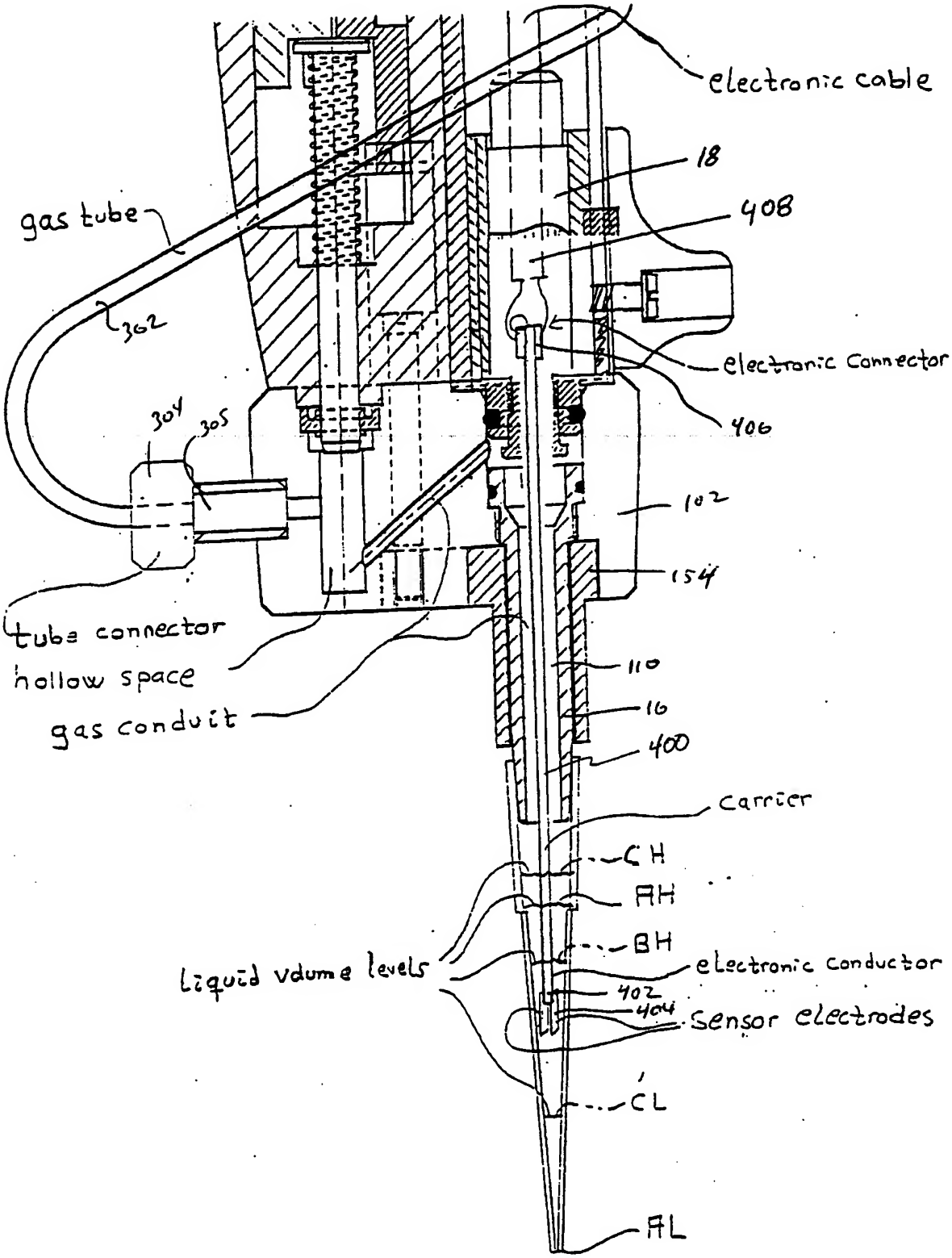
electronic cable
18
408
gas tube
362
electronic Connector
406
304
305
102
154
tube connector
hollow space
gas conduit
110
16
400
carrier
CH
AH
BH
liquid volume levels
electronic conductor
402
404
sensor electrodes
CL
AL

Figure 25

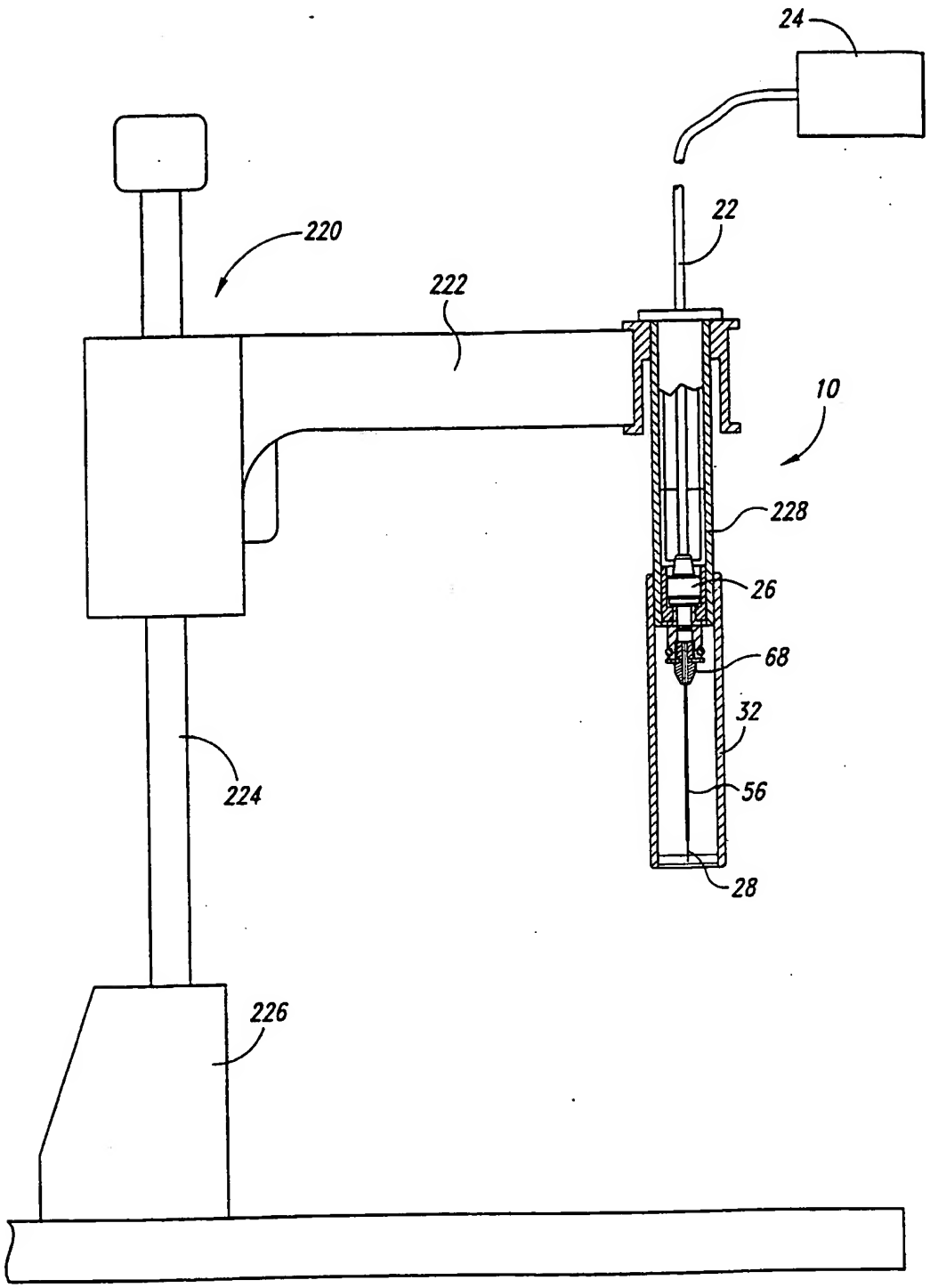

Fig. 26

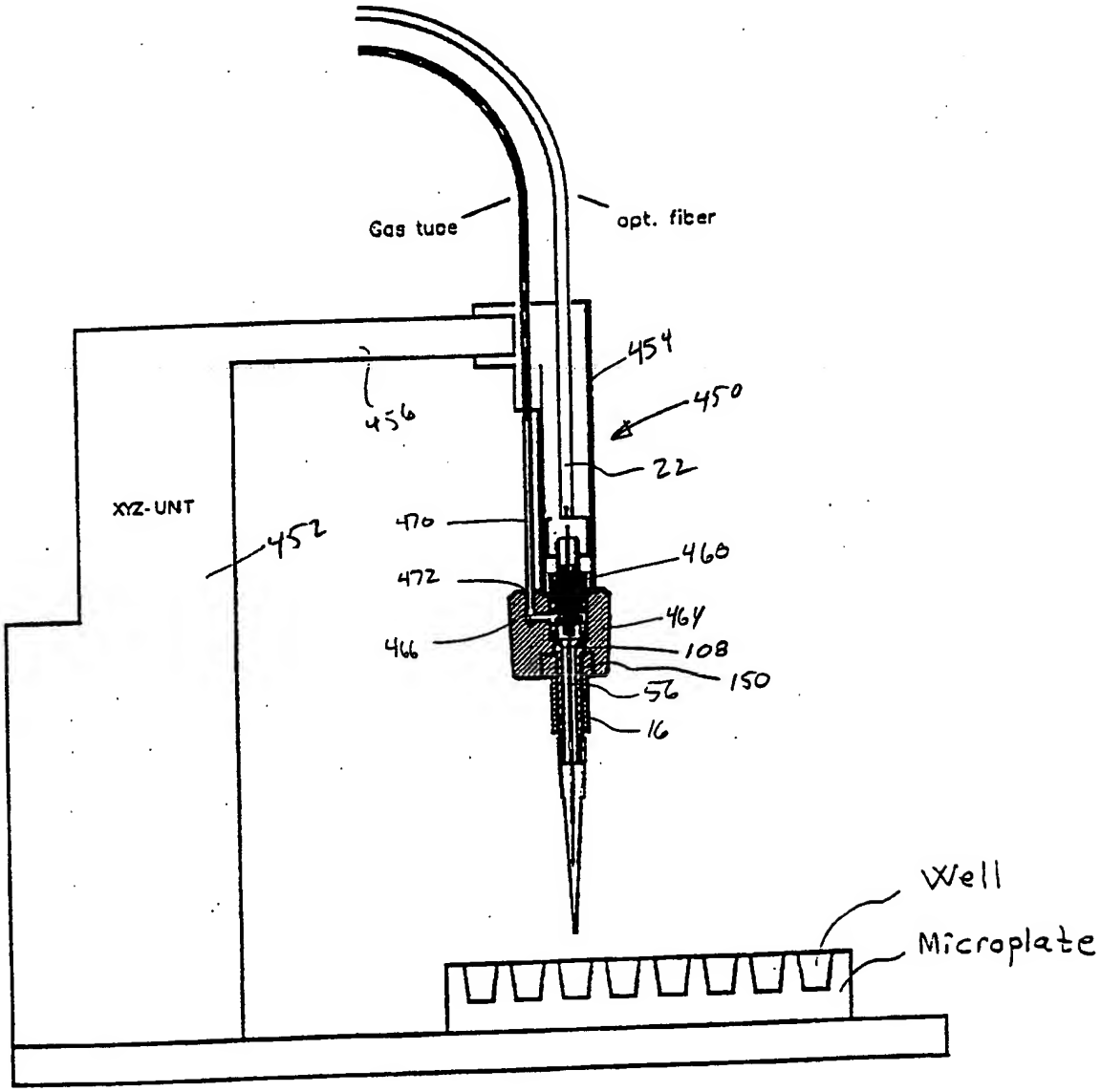
Gas tube
opt. fiber
454
450
456
22
XYZ-UNT
452
470
460
472
464
466
108
150
56
16
Well
Microplate

Figure 27

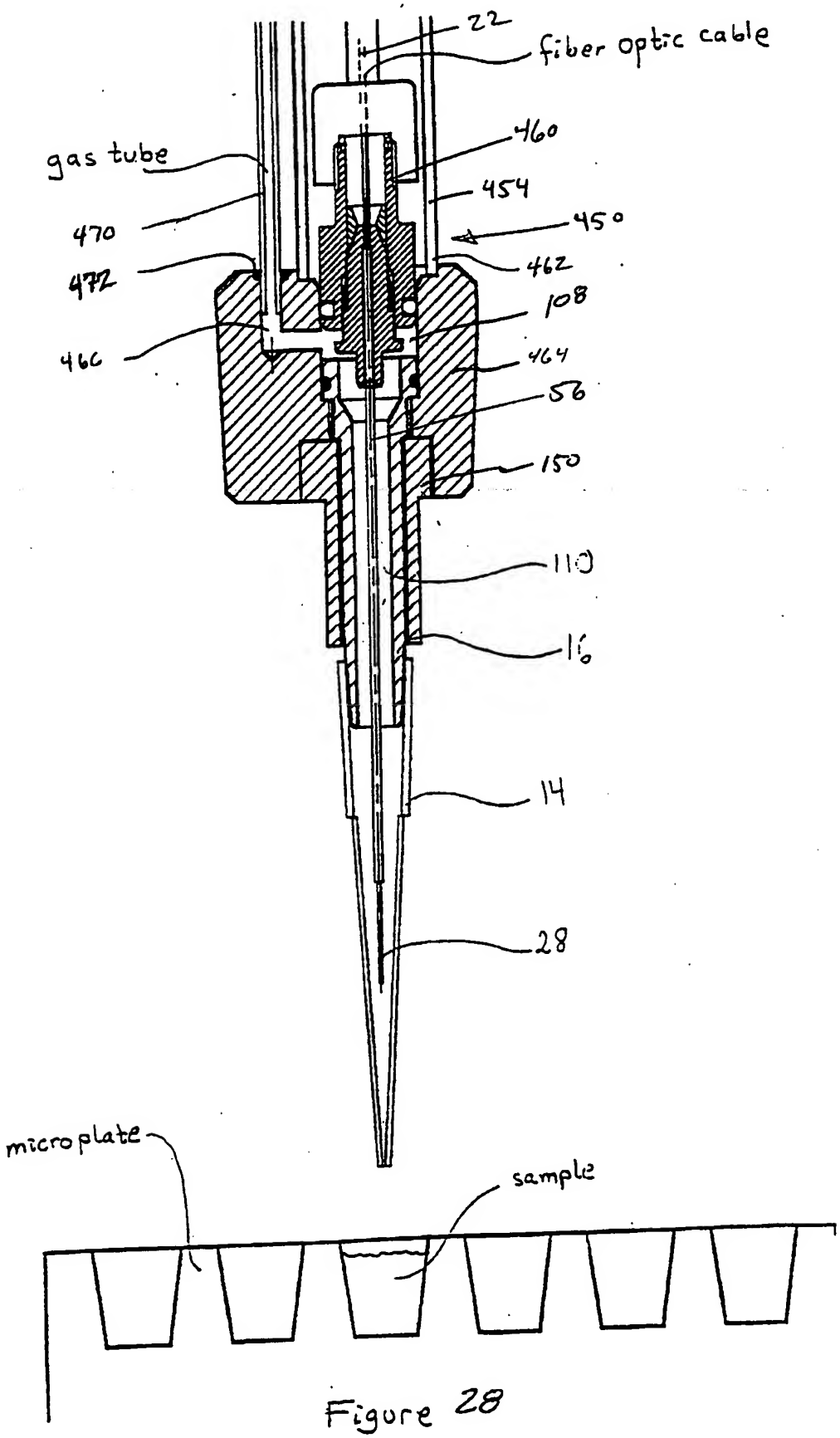
22
fiber optic cable
460
gas tube
454
470
450
462
472
108
466
464
56
150
110
16
14
28
microplate
sample

Figure 28

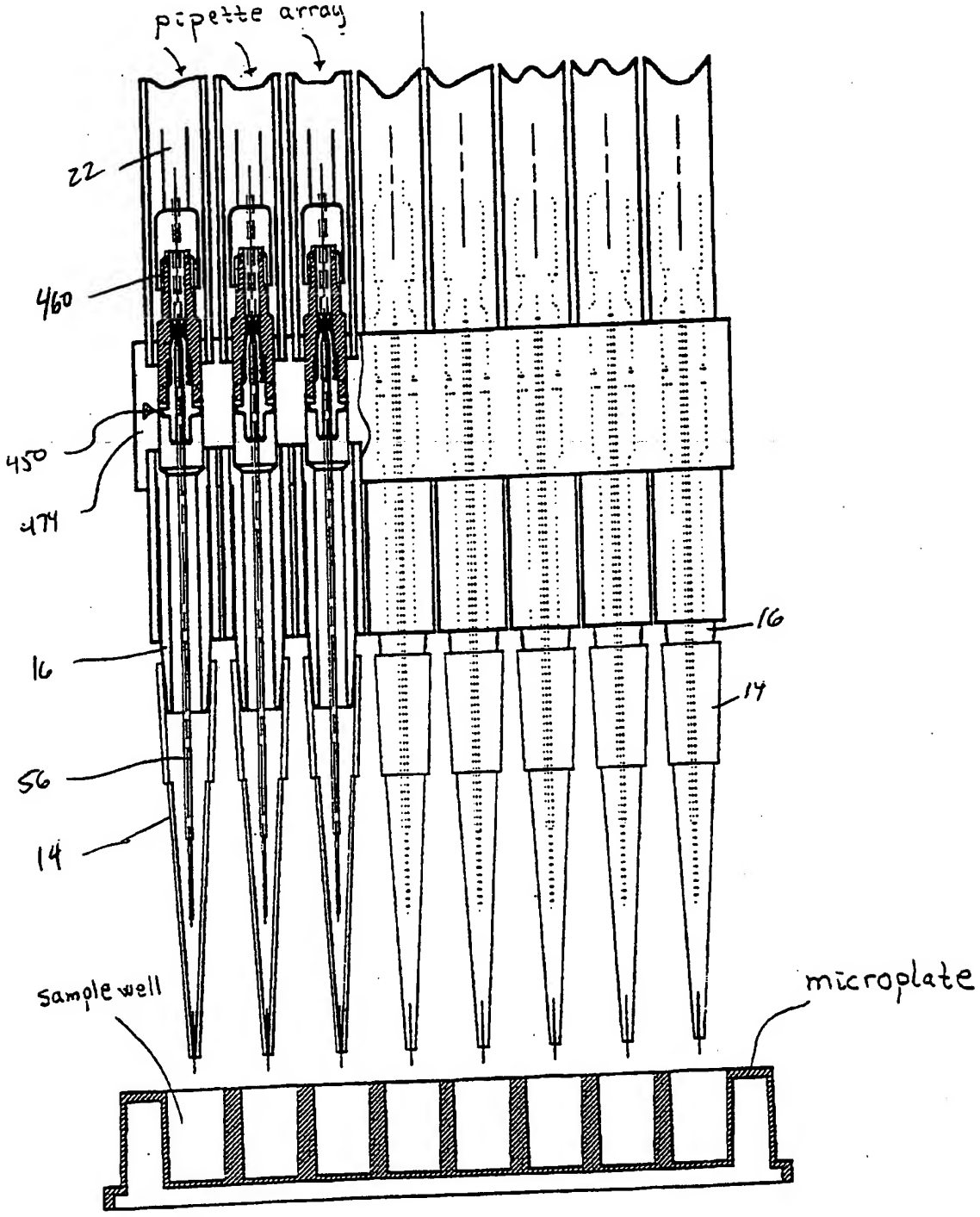
pipette array
22
460
450
474
16
16
14
56
14
sample well
microplate

Figure 29

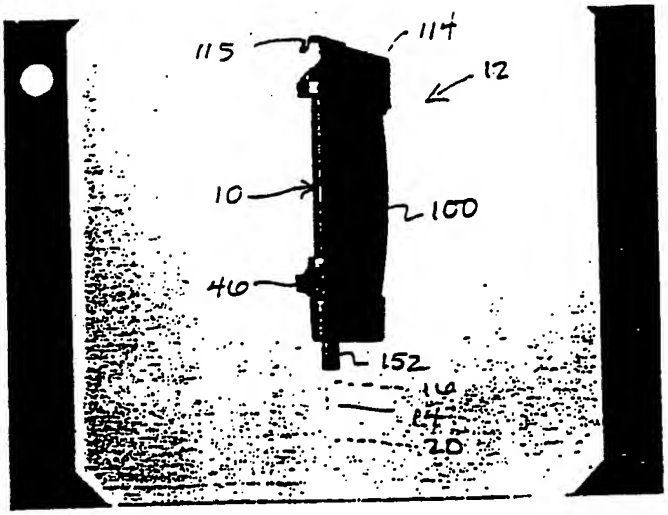

Fig. 30A

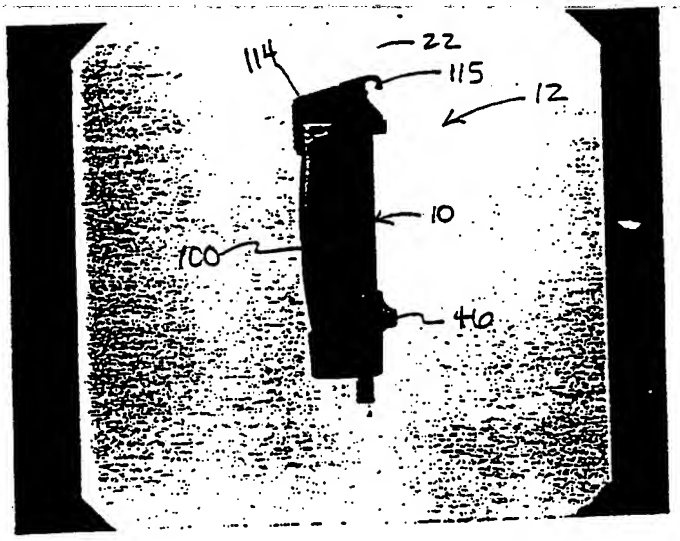

Fig. 30B

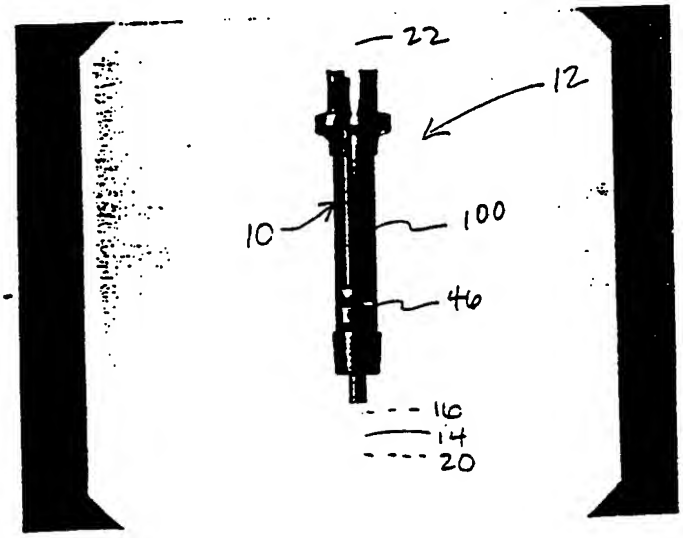

Fig. 30C

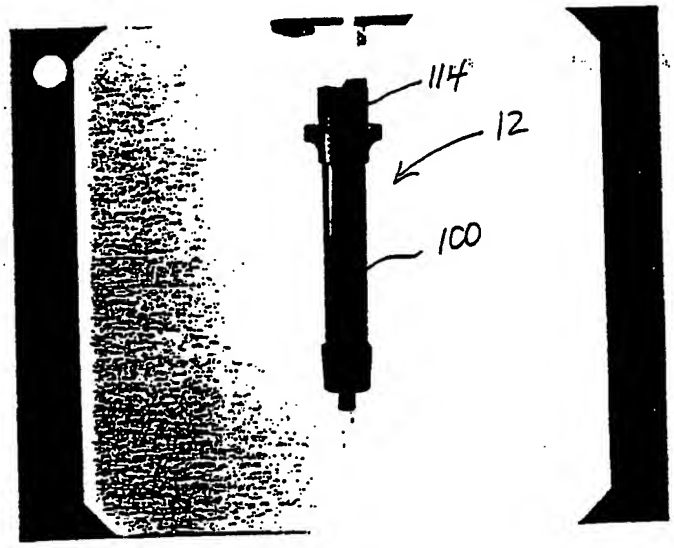

Fig. 30D

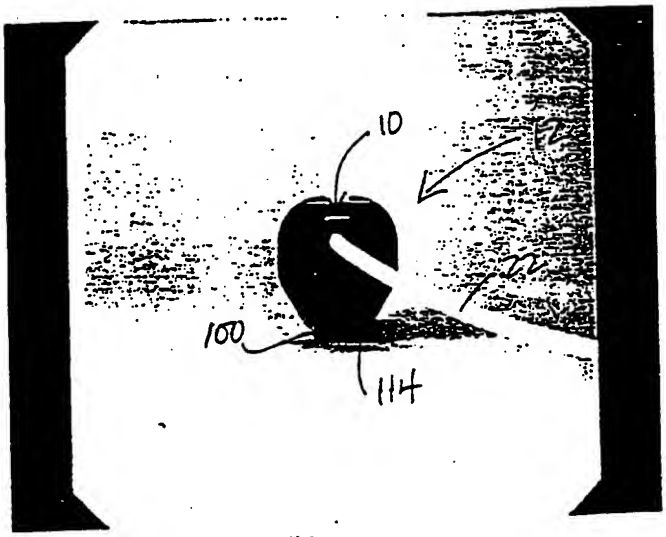

Fig. 30E

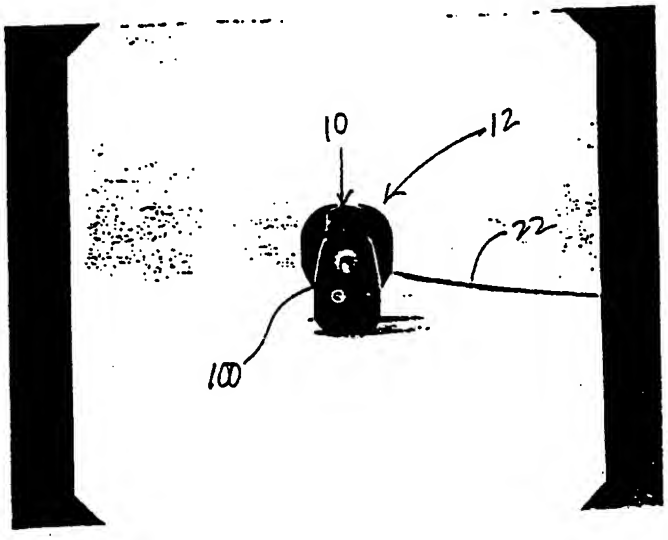

Fig. 30F

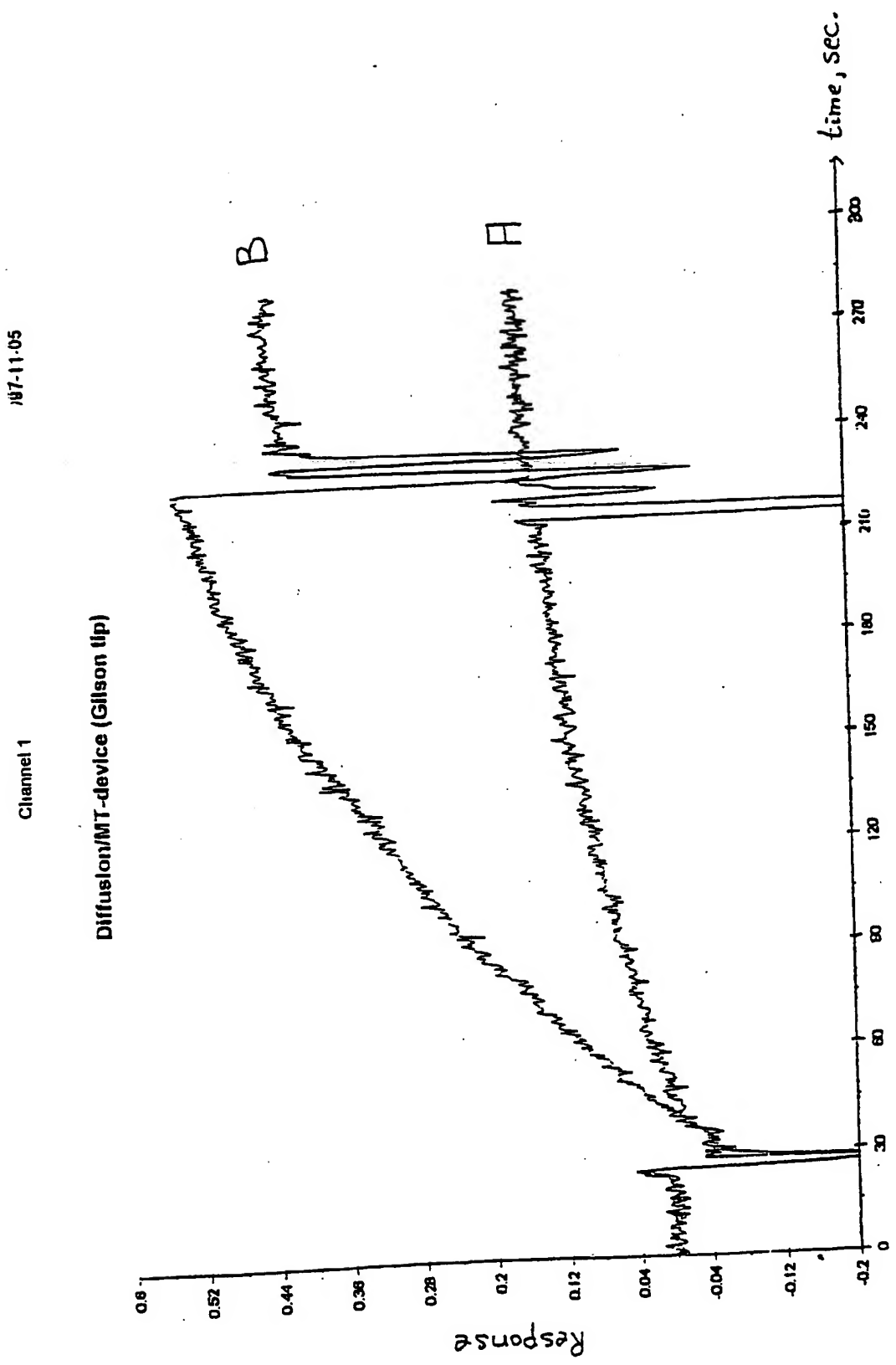
97-11-05
Channel 1
Diffusion/MT-device (Gilson tip)
B
A
Response
time, sec.
0.6
0.52
0.44
0.36
0.28
0.2
0.12
0.04
-0.04
-0.12
-0.2
0
30
60
90
120
150
180
210
240
270
300

Figure 31

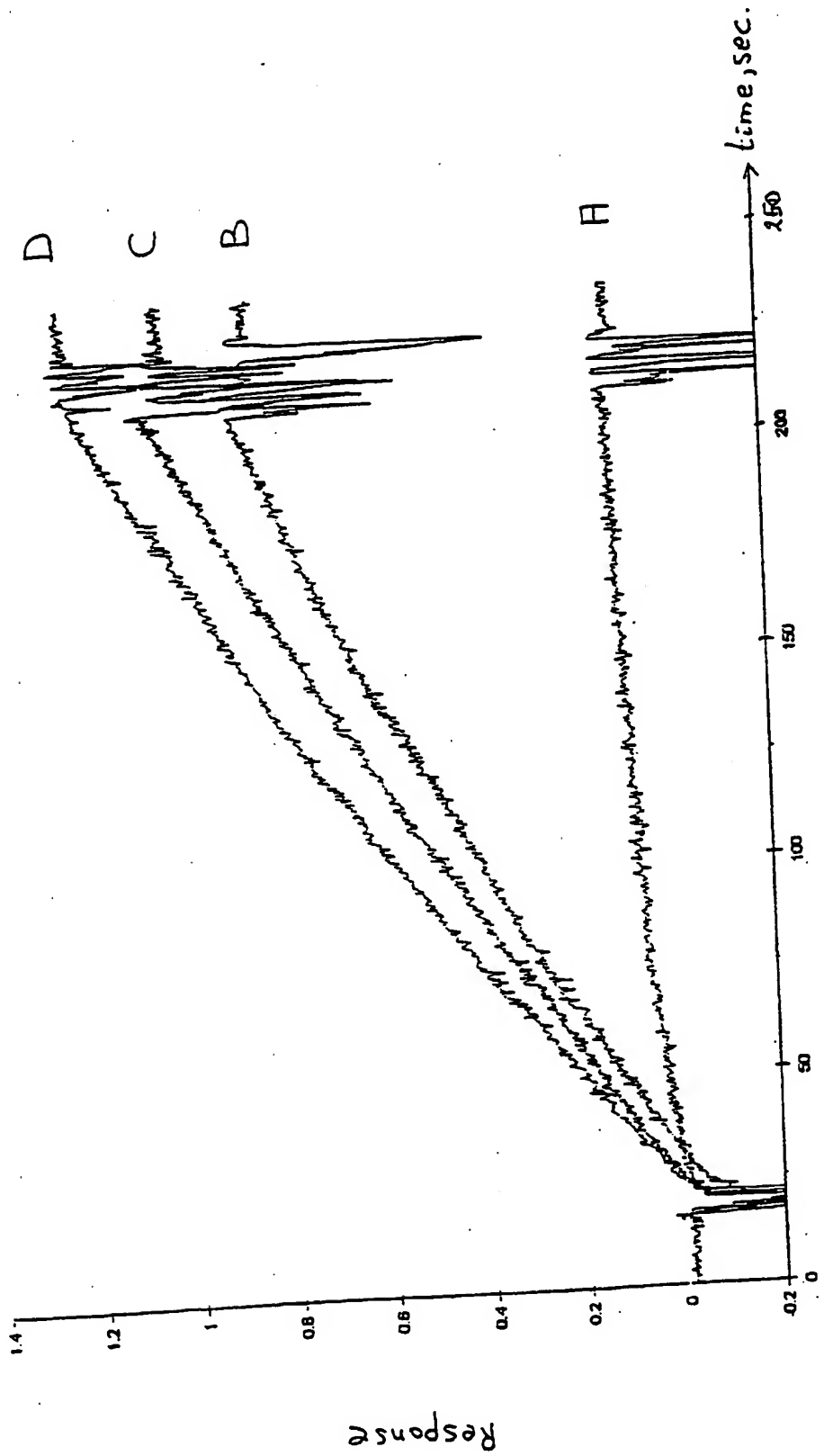
97-11-04
Channel 1
0917: MT - frequency/amplitude (special 11p)
D
C
B
A
Response
time, sec.
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0
50
100
150
200
250

Figure 32A

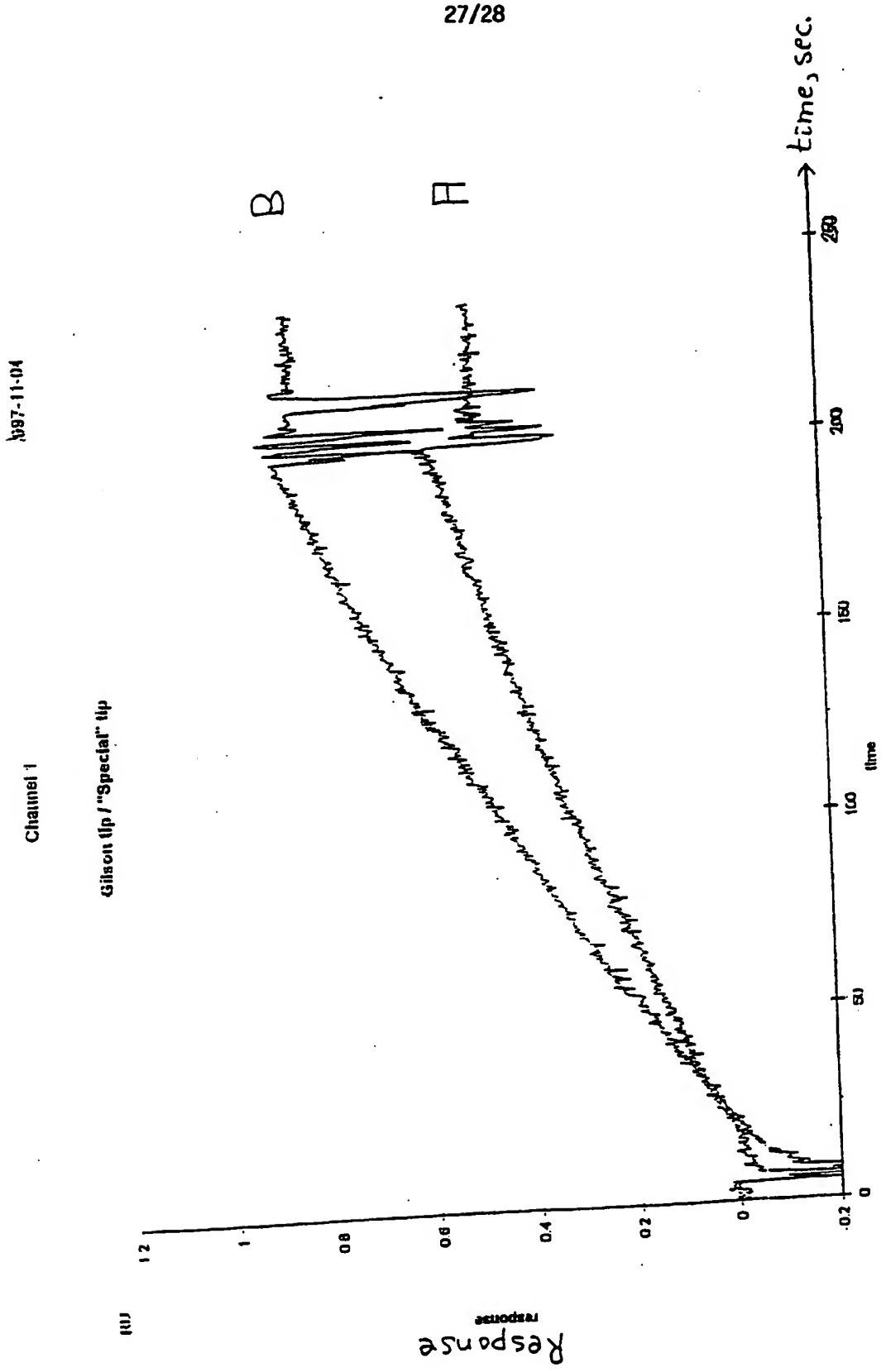
B
A
time, sec.
Response
1997-11-04
Channel 1
Gilson tip / "Special" tip
time

Figure 32B

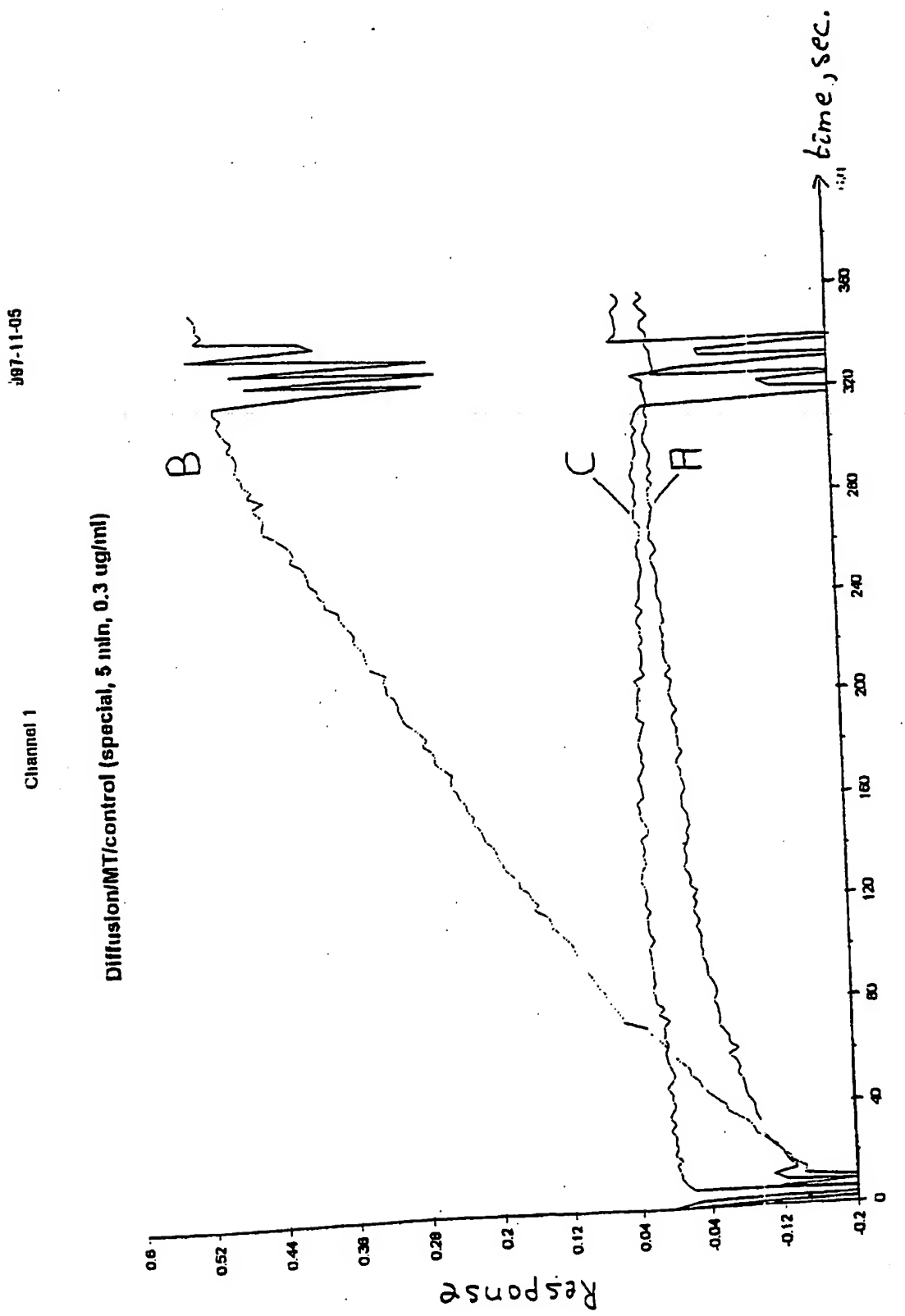
Response
Time, sec.
B
C
A
Channel 1
Diffusion/MT/control (special, 5 min, 0.3 ug/ml)
97-11-05

Figure 32C

INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 98/01370

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N21/03 B01L3/02

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 076 406 A (MILES LAB) 13 April 1983 see page 6, line 19 - page 8, line 25 see claims 1,6,7; figure 2	1-3,15
Y		4,18
A		32

Y	WO 96 37302 A (RAININ INSTR CO INC) 28 November 1996 see claim 1	4
A		6

Y	US 5 359 681 A (JORGENSON RALPH C ET AL) 25 October 1994 cited in the application see claim 1	18
A		1,2

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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25 May 1998	04/06/1998

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2

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 98/01370

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 87 06008 A (BECKMAN INSTRUMENTS INC) 8 October 1987 see page 27, paragraph 2 - page 29, paragraph 1 see page 39, paragraph 3 - page 40, paragraph 3	1,2,15
A	US 4 240 751 A (LINNECKE CARL B ET AL) 23 December 1980 see column 16, line 37 - column 17, line 40 see figures 1,9	1,2,15

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter ional Application No
PCT/US 98/01370

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0076406 A	13-04-1983	US 4488814 A	18-12-1984
		AU 552948 B	26-06-1986
		AU 8707082 A	12-05-1983
		CA 1190408 A	16-07-1985
		CA 1199166 C	14-01-1986
		DE 3278559 A	07-07-1988
		EP 0163826 A	11-12-1985
		JP 58068648 A	23-04-1983
		US 4566203 A	28-01-1986
WO 9637302 A	28-11-1996	US 5614153 A	25-03-1997
		EP 0772493 A	14-05-1997
		JP 10503128 T	24-03-1998
US 5359681 A	25-10-1994	AT 160871 T	15-12-1997
		CA 2153389 A	21-07-1994
		DE 69407161 D	15-01-1998
		DE 69407161 T	26-03-1998
		EP 0678194 A	25-10-1995
		JP 8505475 T	11-06-1996
		WO 9416312 A	21-07-1994
		US 5647030 A	08-07-1997
WO 8706008 A	08-10-1987	EP 0261202 A	30-03-1988
		FI 875113 A	19-11-1987
		JP 8082630 A	26-03-1996
		JP 8054401 A	27-02-1996
		JP 63502931 T	27-10-1988
		US 5104621 A	14-04-1992
		US 5139744 A	18-08-1992
		US 5108703 A	28-04-1992
		US 5125748 A	30-06-1992
		US 5206568 A	27-04-1993
		US 5369566 A	29-11-1994
US 4240751 A	23-12-1980	CA 1122811 A	04-05-1982

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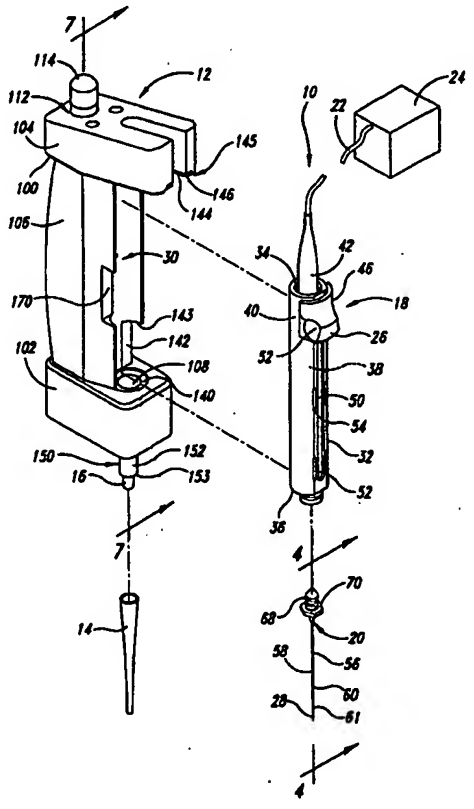
(54) Title: PIPETTE AND CARRIER ASSEMBLY FOR A SENSOR

(57) Abstract

The sensor assembly (10) is releasably attached to the sample drawing device (12), such as a pipette and has a sensor carrier (18) with a coupling member (26) attached to a wave–guide cable (22, 208) connected to the electromagnetic radiation source (204). The sensor (20) has a connecting member (68) connectable to the coupling member and a probe (56) projecting from the connecting member. A probe cover (32) is attached to the coupling member and positionable to selectively expose or protectively contain the probe. The sensor (20) is removably received in a protective storage housing when the sensor is removed from the sensor carrier. The sample drawing device includes a drawing mechanism (112) for drawing a selected sample into a sample container (14) and an ejector (150) for ejection of the sample container (14). The sample drawing device is connected to a pneumatic tube (302) that communicates with the sample container, thereby oscillating the sample within the sample container relative to the sensor.



*(Referred to in PCT Gazette No. 48/1997, Section II)

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PIPETTE AND CARRIER ASSEMBLY FOR A SENSOR

TECHNICAL FIELD

The present invention is generally directed toward analytical detection systems for testing a selected sample, and more specifically, toward a wave-guide based chemical-analytical detection system using a sample drawing device and a wave-guide sensor assembly for selectively providing and testing the sample by electromagnetic radiation propagation to and from the selected sample.

BACKGROUND OF THE INVENTION

Chemical-based analytical detection systems are widely used, particularly in the biochemistry and pharmaceutical industries to detect the presence and/or amounts of selected chemicals, compositions, antibodies, hormones, DNA, analytes, or other reagents within a selected sample. Conventional analytical detection systems that use optical sensing systems include systems using evanescent wave-guide sensors, such as is discussed in U.S. Patent No. 5,105,305. Evanescent wave-guide sensors may utilize various physical phenomenon such as surface plasmon resonance (SPR), interferometry, Fabry-Pe'rot resonance, and fluorescence. The sensors may be based on the sample's light emission (*e.g.*, luminescence, fluorescence, phosphorescence, Raman Spectroscopy, or light scattering on surface-enhanced Raman spectroscopy, including surface-enhanced resonance Raman spectroscopy (*see, e.g.*, U.S. Patent No. 4,781,458), and on evanescent wave surface-enhanced Raman spectroscopy (*see, e.g.*, Keller, R., *Applied Spectroscopy 51, No. 4:* 495-503, 1997). For a comprehensive review of evanescent wave-guide sensors see *Dakin & Culshaw, Optical Fiber Sensors: Principles and Components*, vol. 1, chpt. 6 and 9 (1988*) and Culshaw & Dakin, Optical Fiber Sensors: Systems and Applications*, vol. 2, chpt. 16 (1989). Additionally, evanescent wave-guide sensors may be based on measurement of Brewster angle or detection of polarization state by, for example, ellipsometry, frustrated total reflection mode coupling, ring-resonator mode coupling, and evanescent wave spectroscopy.

Another conventional analytical detection system disclosed in U.S. Patent No. 5,416,879 analyzes light absorbed by a fluid drawn into a liquid-core fiber-optic wave guide, wherein the fluid is drawn into and expelled from the wave-guide by means of a fiber-optic plunger. Still another analytical detection system disclosed in U.S. Patent No. 5,253,037 utilizes light leaking through a discontinuous metal layer on an optical fiber.

Other highly sophisticated and accurate optical sensing systems include surface plasmon resonance (SPR) sensors and related detection equipment that are constructed based upon the Kretschmann configuration. In the Kretschmann configuration, a thin layer of highly reflective metal (such as gold or silver) is deposited on the base of a prism or semicylindrical lens, the metal surface is coated with a selected chemical treatment, and a sample, such as a liquid or a gas, is carefully brought into contact with the coated metal surface.

An SPR reflection spectra of the sample is measured by coupling transverse magnetic polarized, monochromatic light into the prism or lens and measuring the reflected light intensity as a function of either the angle of incidence, or the wavelength of incidence, as effected by surface plasmon waves at the boundary between the metal layer and the chemical sample. These optical sensing systems, in conjunction with appropriate chemical sensing layers, have led to the development of a variety of other SPR-based chemical sensors, including immunoassay sensors (*e.g.*, Liedberg et al., *Sensors and Actuators 4*:299-304, 1983; Daniels et al., *Sensors and Actuators 15*:11-7, 1988; Jorgenson et al., *IEEE/Engineering Medicine and Biology Society, Proceedings 12*:440-442, 1990), gas sensors (Liedberg et al., *supra*; Gent et al., *Applied Optics 29*:2843-2849, 1990), and liquid sensors (*e.g.*, Matsubara et al., *Applied Optics 27*:1160-1163, 1988).

While these SPR-based optical sensing systems are highly accurate, reliable, and sophisticated, the systems are typically large and best suited for simultaneous multi-analyte detection in centrally located sensing applications in the area of the large equipment. Such SPR-based optical sensing systems are not particularly well-suited for remote sensing, so chemical samples drawn by a pipette or the like must be brought to the sensing system to conduct the desired sample analysis. The instrument

disclosed in U.S. Patent No. 5,313,264 is an example of such a SPR-based optical sensing system.

A significant development in analytical detection systems, as disclosed in U.S. Patent No. 5,359,861 (Jorgenson et al., October 25, 1994), provided a fiber optic SPR-based chemical sensor that is connected to an electromagnetic radiation source and a detection device. U.S. Patent No. 5,359,861 is hereby incorporated in its entirety by reference thereto. The fiber optic SPR sensor of Jorgenson et al. includes an optical fiber coupled at one end to the electromagnetic radiation source and the detection device, and the optical fiber's opposite end has a sensing area wherein a section of the optical fiber's core wave guide is exposed by removing a portion of buffer and cladding from the core wave guide. An SPR supporting metal layer is symmetrically deposited around the exposed core wave guide to provide a symmetric sensing area of the SPR sensor. These fiber optic SPR sensors are dipped or otherwise brought into contact with a selected chemical sample.

The electromagnetic radiation source provides multiple wavelength radiation through the fiber optic to the sensing area. The detection device monitors the radiation exiting the optical fiber wave guide, thereby allowing for easy, quick, and highly accurate testing. The fiber optic SPR sensors also permit an inexpensive testing system that allows for remote sensing of samples.

These fiber optic SPR sensors detect the presence or absence of the chemical sample by moving the exposed core wave guide and SPR supporting metal layer into contact with the selected sample. The exposed core wave guide and metal layer are fragile and can be damaged or contaminated if the fiber optic sensor inadvertently impacts rigid structures or contacts a surface having a chemistry different than the sample to be tested. Accordingly, a user must use caution during a sampling procedure with these fiber optic SPR sensors to ensure accurate results and to avoid damaging the sensors.

Other fiber optic-based analytical detection systems are known which do not use the SPR detection technique to detect the presence of a selected component or chemical. As an example, a reservoir fiber optic chemical sensor (FOCS), as is disclosed in U.S. Patent No. 4,892,383, provides a reservoir sensor with a semi-permeable

membrane through which a selected chemical species passes to interact with a selected reagent to analyze the chemical species.

Another example includes fiber-optic phosphorous-based sensors which are used to detect phosphorescent components of a selected sample or fluorescent tags applied to particular components of the sample. The degree of change in light into and out of the fiber optic sensor is monitored in order to detect the presences of the reagent for which the sample is being tested. The fiber-optic sensors are dipped into the selected sample. Accordingly, use of the fiber-optic sensor requires the selected sample be provided in a sample container adapted to receive the fiber-optic sensor.

Pipettes and other conventional sampling devices, such as the "Pipetman" model manufactured by Gilson, are used to draw a controlled volume of the sample into a disposable pipette tip, so the sample can be transferred to a selected container or assembly for testing. After the sample has been transferred, the pipette tip is typically disposed of and replaced with a clean pipette tip into which another sample can be drawn. This process of drawing the sample into a pipette tip and transferring the sample to the selected container assembly for testing is a labor-intensive process, particularly when done repeatedly throughout a testing procedure.

Moreover, the prior art pipettes and other conventional sampling devices are typically used only for sample handling (*i.e.*, drawing sample and/or reagents into the pipette tip for subsequent dispensing). The prior art pipettes are not typically used as reaction chambers or flow cells for use with fiber optic-based analytical detection systems. In these systems, flow cells are generally required to ensure that the concentration of analyte in the proximity of the sensing surface is equal to the bulk analyte concentration at all times. In non-flow or static sample environments, the binding of analyte at the sensing surface can cause an analyte concentration gradient across the sample that impedes mass transfer. An analyte concentration gradient may provide less reliable chemical kinetic information.

While conventional wave-guide based sensors and sampling devices are known, there is still a need for wave-guide based analytical detection systems and sampling methods that are inexpensive, easy and fast to use, that provide simplified, consistent and accurate testing with a high degree of repeatability, and that avoid the

drawbacks of the prior art. There is also a need for an improved wave-guide based sensor of an analytical detection system that is protected from damage or contamination during use of the system. There is further a need for a sample drawing device that is usable in conjunction with such an improved wave-guide based sensor to facilitate efficient, inexpensive, and highly accurate testing of the selected samples. There is still another need for an improved analytical detection system that counteracts sample concentration gradients which tend to impede mass transfer to a wave-guide based sensor.

SUMMARY OF THE INVENTION

The present invention provides a sensor assembly and sample moving mechanism, such as a sample drawing device, that overcome the drawbacks experienced by the prior art and provides further related advantages. In one exemplary embodiment of this invention, the sensor assembly is a wave-guide sensor assembly usable with an electromagnetic radiation source and a wave guide cable has a wave-guide-sensor carrier connectable to the wave guide cable and adapted to removably receive a wave-guide sensor. The wave-guide-sensor carrier is releasably received by a sample drawing device, such as a pipette, which is adapted to allow a selected sample to be tested by the wave-guide sensor when attached to the wave-guide-sensor carrier.

In one embodiment, the wave-guide-sensor carrier includes a wave-guide-coupling member attached to the wave guide cable and a sensor-probe cover attached to the wave-guide-coupling member. The wave-guide sensor is releasably attached to the wave-guide-coupling member. The wave-guide sensor includes a connecting member that attaches to the wave-guide-coupling member, and a sensor probe extends through the connecting member and terminates at a first sensing area spaced apart from the connecting member. The wave-guide-coupling member aligns and optically couples the sensor probe with the wave guide cable for propagating the electromagnetic radiation from the wave guide cable through the sensor probe to the sensing area.

The wave-guide-sensor carrier has a probe cover attached to the wave-guide-coupling member. The wave-guide-coupling member is movable relative to the

probe cover to selectively cover and uncover the sensor probe. The wave-guide-coupling member and sensor probe of the preferred embodiment are movable between a sensor-retracted position with the probe's sensing area contained within the probe cover, and a sensor-extended position with the probe's sensing area being exposed and in a position ready for engaging a selected sample.

The wave-guide sensor assembly includes a protective storage housing that is removably attachable to the wave-guide sensor for storage of the sensor when it is not attached to the wave-guide-coupling member. The storage housing of the preferred embodiment contains the wave-guide sensor therein and protects it from being damaged or contaminated.

In one embodiment, the sample drawing device includes a sensor-carrier-receiving portion that receives the wave-guide sensor assembly when the assembly is in an installed position. The sample drawing device has a locking mechanism that releasably engages to the wave-guide-sensor carrier and retains the wave-guide sensor assembly in the installed position with the sensor probe being aligned with a drawing tube. The drawing tube terminates at a sample-container receiving portion that is shaped to releasably receive a sample container thereon.

The sample drawing device includes a drawing mechanism coupled to the drawing tube and adapted to draw a selected volume of a sample into the sample container for engagement with the wave-guide sensor during a sampling procedure. The sample drawing device includes an ejector coupled to the drawing mechanism and positioned adjacent to the drawing tube's sample container receiving portion. The ejector is movable between a retracted, disengaged position out of engagement with a sample container and an extended, ejection position to eject the sample container from the drawing tube's sample-container receiving portion. The tip ejector is adapted to selectively engage the drawing mechanism so activation of the drawing mechanism moves the ejector between the retracted, disengaged position and the extended, ejection position.

In another embodiment of the present invention, the sensor assembly is mounted on a sensor support device, such as a stand. The sensor is retained in a fixed position relative to the sensor support device and the probe cover is slidably movable

between a lowered, sensor-retracted position and a raised, sensor-exposed position to selectively expose the sensor probe during a sampling procedure. In a further embodiment, a plurality of sensor assemblies are mounted to a support device, for example, so the assemblies can be used simultaneously during a sampling procedure.

In one preferred embodiment of the present invention, the sample drawing device is a hand-held device having a handle, drawing mechanism, sensor-carrier-receiving portion, and testing electronics contained in a housing portion attached to the handle. The testing electronics include a power source, a microprocessor, an electromagnetic radiation source, a detection device, and a wave guide connecting cable adapted to connect the electromagnetic radiation source and detection device to the wave-guide-coupling member when the wave-guide sensor assembly is installed on the sample drawing device. A data display unit is attached to the handle and coupled to the detection device to display sampling results generated by the detection device for a selected sample. Accordingly, the hand-held sample drawing device, such as a pipette, is a self-contained testing unit.

In another embodiment of the present invention, the sample drawing mechanism is an automated drawing mechanism that allows for alternating positive and negative pressure within a drawing tube of the pipette. The alternating pressure within the drawing tube causes liquid sample within a pipette tip, which is connected to the pipette's drawing tube, to fluctuate or oscillate in the pipette tip between an upper level and a lower level. The sample oscillation within the pipette tip counteracts the creation of a concentration gradient within the sample during sensing. In an alternate embodiment, the sample drawing mechanism includes an adjustable air regulation system for controlling the amount of positive and negative pressure applied to the pipette tip.

In another embodiment of the present invention, the pipette has a removable, constricted pipette tip that is positioned in an operative relationship with the wave-guide sensor. In this embodiment, the pipette tip consists of a lower tip portion having a first cross-sectional area, an upper tip portion having a second cross-sectional area, and a constricted middle portion interposed between the lower and upper tip portions and having a third cross-sectional area that is less than either the first or second cross-sectional area of the respective lower and upper tip portions. The pipette tip is

sized so the sensor's sensing area is positioned in the constricted middle portion. The constricted middle portion provides for an accelerated sample flow over the sensor's sensing area as the sample is oscillated due to the venturi effect. Alternatively, the pipette tip consists of two-parts: a first tip-part and a second tip-portions removably attachable to the first tip-portion. The first tip-portion is a micropipette that is adapted to sample volumes of liquid ranging from 2 to 20 microliters inclusive.

In another embodiment of the present invention, the pipette is positioned in an operative relationship with the sensor and is adapted to allow the sensor's sensing area to move laterally within the pipette tip between first and second positions when the volume of a selected sample within the pipette is oscillated.

In an alternate embodiment, the sensor assembly includes a connecting member substantially adjacent to the sensor's input/output end, and the connecting member is attached to an elongated housing that contains the sensor therein. The connecting member has an engagement portion positioned to be engaged, automatically or manually, by the coupling member's sensor receiving portion. A distal end portion of the housing contains the sensor's sensing area therein and is adapted to allow sample to flow through the distal end portion and over the sensing area.

The present invention is also directed toward a method of analytically sampling a selected chemical sample with a wave-guide sensor assembly that is coupled to an analyzer and a source of electromagnetic radiation. The method of one embodiment of the invention includes providing a sensor carrier having a wave-guide receiving member that is coupled to the analyzer and the source of electromagnetic radiation by a wave-guide cable, removably attaching the wave-guide sensor to the wave-guide receiving member, and propagating electromagnetic radiation between the source of electromagnetic radiation and the sensing end portion of the wave-guide sensor through the wave-guide cable and the wave-guide sensor.

This embodiment of the sampling method also includes moving the wave-guide sensor relative to a sensor cover from a sensor contained position, in which the sensing end portion is covered by the sensor cover, to a sensor extended position, in which the sensing end portion is exterior of the sensor cover and exposed. The sample is then contacted with the sensing end portion of the wave-guide sensor. The

electromagnetic radiation propagating through the wave-guide cable from the sensing end portion of the wave-guide sensor is analyzed with the analyzer when the sensing end portion is contacting the sample, thereby analyzing the sample.

The method of one embodiment of the invention further includes the step of withdrawing the waveguide sensor from the sample and moving the wave-guide sensor from the sensor extended position to the sensor contained position with the sensing end portion being covered. After the waveguide sensor has been withdrawn to the sensor contained position, the waveguide sensor is moved to the sensor extended position, and sensing end portion is contacted with a second selected chemical sample.

In another alternate embodiment, the method includes the step of oscillating the sample within the pipette tip relative to the wave-guide sensor when the wave-guide sensor is in the sensor-extended position.

A method of another embodiment of the invention includes moving the selected chemical sample into contact with the sensing end portion of the wave-guide sensor and simultaneously analyzing with the analyzer the sample as it is moved into contact with the sensing end portion of the wave-guide sensor.

These and other aspects of this invention will become evident upon reference to the following detailed description and attached drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a partially exploded isometric view of a pipette and a wave-guide sensor assembly in accordance with a preferred embodiment of the present invention.

Figure 2 is an enlarged isometric view of the wave-guide sensor assembly of Figure 1, the wave-guide sensor assembly having a sensor carrier with a sensor coupling member slidably attached to a probe cover, and a fiber optic sensor connected to the sensor coupling member, the sensor coupling member being shown in solid line in a sensor-retracted position, and shown in phantom line in a sensor-extended position with the fiber optic sensor partially extending from the probe cover and shown in phantom line in an intermediate position between the sensor-retracted and sensor-extended positions.

Figure 3 is an enlarged cross-sectional view taken substantially along line 3-3 of Figure 2 showing the sensor carrier and the fiber optic sensor.

Figure 4 is an enlarged cross-sectional view taken substantially along line 4-4 of Figure 1 showing the fiber optic sensor.

Figure 5 is an isometric view of a protective storage housing removably containing the fiber optic sensor of Figure 4, with a closed-end tubular cover shown in phantom line.

Figure 6 is an enlarged cross-sectional view taken substantially along line 6-6 of Figure 5 showing the storage housing and the fiber optic sensor.

Figure 7 is an enlarged cross-sectional view taken substantially along line 7-7 of Figure 1 showing the pipette.

Figure 8 is a cross-sectional view of the pipette similar to Figure 7 with the sensor carrier of Figure 2 being shown in an installed position, a pipette tip being shown mounted on the pipette, the sensor coupling member and fiber optic sensor being shown in solid line in the sensor-extended position and shown in phantom line in the sensor-retracted position.

Figure 9 is a cross-sectional view of the pipette of Figure 8 with the sensor coupling member and fiber optic sensor shown in the intermediate position, a tip ejector of the pipette being shown in an ejection position, and the pipette tip being shown ejected from the pipette.

Figure 10 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a drawing mechanism operatively coupled to a pipette tip mounted on the pipette.

Figure 11 is an enlarged cross-sectional view of the pipette tip of Figure 10 shown with the sample level within the pipette tip at three different levels.

Figure 12 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a drawing mechanism operatively coupled to a pipette tip mounted on the pipette.

Figure 13 is a cross-sectional view of a constricted pipette tip of an alternate embodiment of the present invention, the pipette tip being shown mounted on the pipette.

Figure 14 is an enlarged cross-sectional view of a pipette tip of an alternate embodiment of the constricted pipette tip similar to the one shown in Figure 13, but with an elongated middle constricted portion.

Figure 15 is a cross-sectional view of a pipette tip of an alternate embodiment of the present invention, a two-part pipette tip being shown mounted on the pipette.

Figure 16 is a cross-sectional view of an alternate embodiment similar to the one shown in Figure 15, but with a shorter second tip-portion.

Figure 17 is a cross-sectional view of a pipette tip of an alternate embodiment of the present invention, the pipette tip being shown mounted on the pipette with the fiber optic sensor in the sensor-extended position and in a laterally off-set position, the sample level within the pipette tip being at an upper level.

Figure 18 is a cross-sectional view of the pipette tip of Figure 17 with the fiber optic sensor in the sensor-extended position and in an axially aligned position, the sample level within the pipette tip being at a lower level.

Figure 19 is a cross-sectional view taken substantially along line 19-19 of Figures 17 and 18 showing the fiber optic sensor in the lateral position and the axially-aligned position of Figure 17 and Figure 18, respectively.

Figure 20 is a cross-sectional view of a pipette of an alternate embodiment of the present invention with a fiber optic spectrograph contained in a housing portion and a data display on the pipette handle.

Figure 21 is a partial cross-sectional view of an alternate embodiment having a pipette regulating assembly with a piston that controls positive and negative pressure transmitted to the pipette tip.

Figure 22 is a partial cross-sectional view of an alternate embodiment having a pipette with a quick release sensor assembly and an adjustable regulating assembly with a piston and an adjustable stop to control the positive and negative pressure transmitted to the pipette tip.

Figure 23 is a partial cross-sectional view of an alternate embodiment having a pipette with regulating assembly with bellows that control the positive and negative pressure transmitted to the pipette tip.

Figure 24 is a cross-sectional view of the quick-release sensor assembly of Figure 23 with a sensor probe contained within a housing.

Figure 25 is a partial cross-sectional view of an alternate embodiment having a pipette with an electrochemical sensor thereon.

Figure 26 is a side elevation view of an alternate embodiment of the present invention showing a sensor assembly mounted on a stand.

Figure 27 is a side elevational view of an alternate embodiment of the present invention showing a sensor assembly mounted on a stand for automatic pipette positioning and automatic sample handling.

Figure 28 is an enlarged partial cross-sectional view of the sensor assembly of Figure 27.

Figure 29 is a side elevational view of an alternate embodiment with a plurality of sensor assemblies mounted on a support structure.

Figures 30A-F are left, right, front, rear, top, and bottom elevation views, respectively, of an alternate embodiment of the present invention.

Figure 31 is comparative experimental data for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10 and 11.

Figures 32A-C are comparative experimental data for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10, 11, and 13.

DETAILED DESCRIPTION OF THE INVENTION

The invention is directed toward a sensor assembly having a sensor carrier and a sensor therein that is usable in sampling a selected sample contacted by the sensor. The present invention is also directed toward a sample-drawing device, such as a pipette or the like, that releasably receives the sensor assembly for use during sampling or testing procedure.

In exemplary embodiments of the invention discussed herein, the sensor is a wave-guide sensor, although the invention also applies to other sensors, such as electrochemical sensors, surface acoustic sensors, transmission absorption sensors, and

the like. The wave-guide sensor is a fiber optic sensor removably connected to the wave-guide-sensor carrier for interchangeability with other fiber optic sensors. The wave-guide sensor carrier and fiber optic sensor are releasably received by the sample-drawing device and positionable to allow the fiber optic sensor to contact a sample drawn by the sample-drawing device. The wave-guide sensor assembly and sample-drawing device advantageously combine a wave-guide sensor with a sample-drawing device in a configuration that allows for inexpensive, fast, simple, accurate testing of selected samples with a high degree of repeatability.

A wave-guide sensor assembly 10 and a pipette 12 in accordance with a preferred embodiment of the present invention are shown in the figures for illustrative purposes. The pipette 12 releasably receives the wave-guide sensor assembly 10 therein and is adapted to draw a selected chemical sample, into a pipette tip 14 that removably attaches to a drawing tube 16 of the pipette 12. The wave-guide sensor assembly 10 is positioned and adapted to test the sample while the pipette tip 14 is on the pipette's drawing tube 16.

The wave-guide sensor assembly 10 includes a fiber-optic-sensor carrier 18 that is connected to a conventional fiber optic spectrograph 24 by a fiber-optic cable 22. The sensor carrier 18 releasably receives and optically couples a fiber optic sensor 20 to the fiber optic cable 22 and to the fiber optic spectrograph 24. The sensor carrier 18 moves the sensor 20 between a sensor-retracted position, wherein the sensor is protectively contained within the sensor carrier, and a sensor-extended position, wherein a portion of the sensor is exterior of the sensor carrier and exposed for a sampling procedure.

When the wave-guide sensor assembly 10 is installed on the pipette 12 and the sensor 20 is in the sensor-extended position, the sensor extends through the pipette's drawing tube 16 and a sensing area 28 of the sensor engages the sample drawn into the pipette tip 14. In the preferred embodiment, the sample is analyzed as the sample is being drawn into the pipette tip 14 while the pipette tip is on the pipette 12. The fiber optic spectrograph 24 is used to detect the characteristics of the sample contacted by the sensor's sensing area 28 by the propagation of multiple-wavelength

electromagnetic radiation through the sensor 20 and the fiber optic cable 22 between the sensor's sensing area 28 and the fiber optic spectrograph.

In the preferred embodiment, the sensor 20 is an SPR-based fiber optic sensor, although other wave-guide sensors are used with the sensor carrier 18 in alternate embodiments. The sensor carrier 18 includes an optical fiber coupling member 26 that releasably receives the sensor 20 and that is connected to the fiber optic cable 22. In one embodiment the coupling member 26 is permanently connected to the fiber optic cable 22, and in another embodiment the coupling member 26 is releasably connected to the fiber optic cable. The coupling member 26 coaxially aligns and operatively couples the sensor 20 to the fiber optic cable 22 to allow for efficient propagation of the electromagnetic radiation through the fiber optic cable and the sensor.

The pipette 12 of the preferred embodiment includes a carrier-receiving portion 30 that releasably receives the sensor carrier 18 in an installed position so the coupling member 26 and sensor 20 are coaxially aligned with the pipette's drawing tube 16. In an alternate embodiment, the sensor carrier 18 is integrally connected to the pipette 12. Accordingly, the pipette 12 and sensor carrier 18 form a unitary hand-held sampling device to which the fiber optic cable 22 and the sensors 20 attach for sampling of the sample.

The sensor carrier 18 includes a probe cover 32 that mounts into the pipette's carrier-receiving portion 30 and that slidably contains the carrier's coupling member 26. The coupling member 26 is slidable relative to the probe cover 32 and relative to the pipette 12 between a sensor-retracted position, wherein the sensor 20 is fully contained within the probe cover, and a sensor-extended position, wherein at least a portion of the sensor extends from the probe cover so the sensing area 28 is exterior of the probe cover to engage the selected sample.

The wave-guide sensor assembly 10 and pipette 12 of the present invention are usable for inexpensive, fast, efficient and highly repeatable sampling of selected chemical samples, while minimizing the amount of equipment and time needed and minimizing the risk of damage to the equipment. Further, the sensor 20 is easily removable from the coupling member 26 so different wave-guide sensors can quickly be

installed in the sensor carrier 18 for sampling different samples with a minimum amount of preparation time.

As best seen in Figures 2 and 3, the sensor carrier's probe cover 32 of the illustrated embodiment is a substantially cylindrical tube having an open top end 34, an open bottom end 36, and an interior area 38 extending therebetween that contains the carrier's coupling member 26. An end fitting 42 of the fiber optic cable 22 is attached to the coupling member 26 and the fiber optic cable extends through the probe cover's open top end 34.

The coupling member 26 includes a cylindrical body portion 40 fixedly attached to the cable's end fitting 42 and a threaded sensor-receiving portion 44 (Figure 3) coaxially aligned with the cable's end fitting. The threaded sensor-receiving portion 44 removably receives the sensor 20 therein and operatively couples the sensor to the fiber optic cable 22 with minimum signal loss or degradation.

The coupling member 26 also has a gripping portion 46 that is slidably positioned on the exterior of the probe cover 32. The gripping-portion is shaped and sized to be gripped by the fingers of a user for movement of the coupling member 26 between the sensor-retracted position, shown in solid line, and the sensor-extended position, shown in phantom line. The gripping portion 46 is securely attached to the coupling member's body portion 40 by a fastener 48 (Figure 3) that extends through an elongated slot 50 in the probe cover 32. The slot 50 extends partially between the open top and bottom ends 34 and 36 of the probe cover 32.

When the coupling member 26 is in the sensor-retracted position, it is adjacent to the probe cover's open top end 34, and the sensor 20 attached to the coupling member is fully contained within the probe cover 32 and protected from being damaged or inadvertently contaminated. When the coupling member 26 is in the sensor-extended position, the coupling member's body portion 40 is within the probe cover's interior area 38 adjacent to the open bottom end 36, and the threaded sensor-receiving portion 44 extends through the open bottom end and terminates at an end exterior of the probe cover 32. The sensor 20 attached to the coupling member 26 is also exterior of the probe cover 32 and ready for sampling the selected sample.

As the coupling member 26 moves between the sensor-retracted and sensor-extended positions, the coupling member's body portion 40 moves axially through the probe cover's interior area 38, and the gripping portion 46 slides along the outside surface of the probe cover.

The probe cover 32 has detent apertures 52 adjacent to the elongated slot 50 near the probe cover's open top and bottom ends 34 and 36. The detent apertures 52 are releasably engaged by the gripping portion 46 of the coupling member 26 to positively retain the coupling member in the respective sensor-retracted and sensor-extended positions. The coupling member's body portion 40 and the gripping portion 46 also frictionally engage the probe cover 32. Accordingly, the coupling member 26 and the sensor 20 attached thereto will remain in any selected position between the sensor-retracted and sensor-extended positions, so the coupling member and the sensor will not inadvertently drop to the sensor-extended position.

The probe cover 32 of the preferred embodiment also has a set of intermediate detent apertures 54 adjacent to the elongated slot 50 at an intermediate position between the other detent apertures 52. The intermediate detent apertures 54 releasably retain the coupling member 26 and the sensor 20 in the intermediate position, shown in phantom line in Figure 3 between the sensor-retracted position and the sensor-extended position. When the wave-guide sensor assembly 10 is installed on the pipette 12 and the coupling member 26 and sensor 20 are in the intermediate position, the sensor's sensing area 28 is fully contained within the pipette's drawing tube 16 so the drawing tube protects the sensing area from damage or inadvertent contamination. Therefore, the sensor's sensing area 28 is protected when the wave-guide sensor assembly 10 is installed on the pipette 12 and the coupling member 26 is in either the sensor-retracted position, the intermediate position, or any position therebetween.

When the wave-guide sensor assembly 10 is removed from the pipette 12, the coupling member 26 and the sensor 20 are in the sensor-retracted position, as discussed in greater detail below, so the sensor's sensing area 28 is protected from damage or inadvertent contamination.

As best seen in Figure 4, the preferred SPR-based fiber optic sensor 20 includes a probe 56 formed by a solid core wave guide 58 comprising the fiber optic

core, fiber optic cladding layer 60, and fiber optic buffer layer 61 which extends from an input/output end 66 and terminates at a terminal reflection end 62. The buffer layer 61 and cladding layer 60 are removed exposing the core for a selected length. Deposited around the exposed core is a layer of an SPR supporting metal forming the sensing area 28. The terminal reflection end 62 is defined by an end face of the core wave guide 58 in contact with a reflective layer 64 that does not support SPR.

The core wave guide's input/output end 66 receives the electromagnetic radiation propagated through the fiber optic cable to the sensor, and the electromagnetic radiation propagates to the terminal reflection end 62 by total internal reflections in the core wave guide 58. The electromagnetic radiation is reflected off the reflective layer 64 in contact with the end face of the core wave guide 58, and propagates back down the core wave guide by the total internal reflections to the input/output end 66. The fiber optic spectrograph's detection device monitors the electromagnetic radiation entering and exiting the input/output end 66 of the core wave guide 58 to determine the results of the selected test or sampling.

The sensor 20 includes a threaded connecting member 68, preferably formed by an injection molded, substantially rigid plastic that is attached to the fiber optic probe 56 adjacent to the input/output end 66. The connecting member 68 has external threads sized to threadably connect to the coupling member's sensor-receiving portion 44 (Figure 3) by being screwed into the sensor-receiving portion. As the sensor's connecting member 68 is screwed into a fully engaged position, the input/output end 66 of the fiber optic probe 56 is positioned immediately adjacent to and coaxially aligned with the end fitting 42 of the fiber optic cable 22 to allow propagation of the electromagnetic radiation into and out of the fiber optic probe. Accordingly, the fiber optic probe 56 is easily and quickly coupled to the fiber optic cable 22 by screwing the sensor's connecting member 68 into the sensor-receiving portion 44 of the coupling member 26.

As best seen in Figure 4, the connecting member 68 of the preferred embodiment is secured to the fiber optic probe 56 by crimping the connecting member onto the buffer layer 61. As the connecting member 68 is crimped onto the buffer layer 61, the end of the connecting member 68 is flush with the end of the core wave guide 58.

Accordingly, the input/output end 66 of the core wave guide 58 is substantially coplanar with the end of the connecting member 68 for efficient propagation of light through the fiber optic probe 56 with a minimum degree of signal loss.

In an alternate embodiment, the input/output end 66 of the core wave guide 58, which is a silicon wave guide, is recessed within the buffer layer 61 by approximately 100 microns. The end of the buffer layer 61 abuts the end fitting 42 of the fiber optic cable 22, and the silicon wave guides are out of direct engagement with each other. The recessed input/output end 66 of the sensor 20 still provides an efficient coupling between the fiber optic cable and the sensor.

In another alternate embodiment, the sensor 20 is a bare fiber sensor without the connecting member 68 at the input/output end. The coupling member 26 in this alternate embodiment is a bare fiber coupler that removably receives the input/output end of the sensor and aligns the sensor's core wave guide with the fiber optic cable 22 for efficient propagation of electromagnetic radiation between the fiber optic cable and the sensor.

When the sensor 20 is not installed on the coupling member 26 (Figure 3), the sensor 20 is stored in a protective storage housing 72 illustrated in Figure 5. The storage housing 72 is a substantially cylindrical tube shaped and sized to fully contain the sensor 20 therein and to protect the sensor's connecting member 68 and sensing area 28 from being inadvertently impacted, damaged, or contaminated. The storage housing 72 is open at both ends so the storage housing and sensor 20 can be packaged as a unit, for example, in a nitrogen gas environment or other selected environment that is best for protecting and storing the sensor before it is used.

The storage housing 72 of the preferred embodiment is a plastic tube that is adapted to be color coded by labels or by forming the storage housing from a plastic material of a selected color. Such color coding of the storage housing 72 allows different types of sensors 20 having different sensing characteristics to be contained in different colored storage housings for easy identification of the sensors.

As best seen in Figures 5 and 6, the storage housing 72 includes an interior flange 74 extending across the housing's interior area near one end of the housing. The interior flange 74 has a central aperture 76 that receives the fiber optic

probe 56 therethrough, and a hexagonal-shaped recessed portion 78 is formed around the central aperture. The recessed portion 78 is sized to receive a mating hexagonal flange 70 on the sensor's connecting member 68 so the hexagonal flange 70 snaps into the recessed portion and into engagement with the storage housing's flange 74. Accordingly, the interior flange 74 releasably retains the sensor 20 within the storage housing 72.

The storage housing 72 is sized to fit into the carrier's probe cover 32 (Figure 3) and to position the connecting member 68 adjacent to the sensor coupling member 26. Installation of the sensor 20 is performed by placing the storage housing 72 with the sensor 20 therein into the probe cover's interior area 38 until the threaded portion of the sensor's connecting member 68 partially engages the receiving portion 44 of the coupling member 26. The storage housing 72 and the sensor 20 are then rotated as a unit, whereby the sensor's connection member 68 is screwed into engagement with the receiving portion 44. The hexagonal-shaped recess 78 in the storage housing 72 acts as a wrench mechanism that engages the connecting members hexagonal flange 70 for easy installation of the sensor 20 into the coupling member 26 to ensure secure engagement and proper alignment of the sensor. After the sensor 20 has been screwed into the installed position, the storage housing 72 is pulled out of the probe cover 32 so the sensor's hexagonal flange 70 is pulled out of the hexagonal recess 78 of the storage housing's flange 74.

The storage housing 72 of the preferred embodiment has a step configuration with a narrower end portion 81 adjacent to the sensing area 28 when the sensor 20 is contained in the housing and a wider end portion 83 adjacent to the sensor's connecting member 68. This step configuration allows a closed-end tube 85, shown in phantom lines in Figure 5, to be mounted onto the narrower end portion 81 so as to cover and close-out the one end of the storage housing 72. The closed-end tube 85 provides additional protection for the sensor 20 and allows the sensor's sensing area 28 to be stored in a selected liquid environment when the sensor is not in use.

As best seen in Figure 5, the narrower end portion 81 of the storage housing 72 has a plurality of rib portions 80 around the exterior of the storage housing. These rib portions 80 provide a gripping surface on the exterior of the storage housing

72 to facilitate rotation of the storage housing and the sensor for installation and removal of the sensor.

In an alternate embodiment, the storage housing 72 is an elongated tubular member with a substantially constant outer diameter, and the storage housing does not have the step configuration. This non-step configuration is easy and inexpensive to manufacture. The end of the storage housing 72 opposite the interior flange 74 is provided with the rib portions 80 to form the gripping surface.

The sensor 20 is removed from the coupling member 26 by moving the storage housing 72 into the probe cover's interior area 38 over the fiber optic probe 56, and pressing the storage housing's flange 74 against the sensor until the hexagonal flange 70 snaps into the hexagonal recess 78. The storage housing 72 and the sensor 20 are then rotated as a unit, the sensor fully unscrewed from the coupling member, and the storage housing and sensor removed as a unit from the probe cover 32. The carrier's coupling member 26 is then ready to receive a different sensor 20. Accordingly, a first sample may be sampled with one sensor when in the sensor-extended position. The sensor is then withdrawn to the sensor-retracted position, removed from the coupling member, and a second sensor is installed for sampling other samples. This replacement of sensors 20 is a very quick and easy procedure.

While the preferred embodiment of the wave-guide sensor assembly 10 is described with respect to the fiber optic sensor 20 coupled to the fiber optic cable 22, the present invention is also applicable to other wave-guide sensors, such as planar wave-guide sensors or the like, usable with a wave guide cable and with an electromagnetic radiation source for propagation of the electromagnetic radiation to and from the wave-guide sensor. In addition, the preferred embodiment utilizes the threadable engagement between the sensor 20 and the coupling member 26, although other interconnections between the sensor and the coupling member such as the bare fiber couplers are available to quickly, easily, and efficiently couple the sensor with the fiber optic cable 22.

As best seen in Figure 7, the pipette 12 of the preferred embodiment is a hand-held sampling device that includes the carrier-receiving portion 30 that is defined by a concave semicylindrical surface integrally formed in a pipette handle 100. The

handle 100 has a bottom portion 102, which defines a bottom end of the carrier-receiving portion 30, and a top portion 104, which defines the upper end of the carrier-receiving portion. A main body portion 106 of the handle 100 extends between the top and bottom portions 104 and 102, and the concave semicylindrical surface is formed in the handle's body portion.

The drawing tube 16 projects away from the handle's bottom portion 102 from a surface opposite the carrier-receiving portion 30. The handle's bottom portion 102 has a sensor-assembly receiving aperture 108 therein open to the carrier-receiving portion 30 and connected to an interior passageway 110 extending through the drawing tube 16. The sensor-assembly receiving aperture 108 is coaxially aligned with the interior passageway 110 and the carrier-receiving portion 30.

The pipette 12 has a drawing mechanism 112 extending through the handle 100 and operatively coupled to the drawing tube 16 to create a selected partial vacuum within the interior channel 110 for drawing a selected volume of a sample into the pipette tip 14 (Figure 1) mounted on the drawing tube 16. In an alternate embodiment, the drawing mechanism 112 is a sample handling device that also creates a selected positive pressure within the interior channel 110 for moving the sample axially in the pipette tip 14 away from the drawing tube 16, and if desired out of the pipette tip 14. Accordingly, the drawing mechanism is broadly defined herein as a device that generates negative and positive pressures that move the sample axially in the pipette tip14. The drawing mechanism 112 has an adjustable thumb-actuated plunger 114 that projects through the handle's top portion 104 and connects to an interior piston 116 that is slidably positioned within a cylinder 120 formed in the handle's body portion 106. The plunger 114 is ergonomically positioned so that a user grasping the handle's body portion 106 can easily and comfortably access the plunger with his or her thumb in order to depress the plunger from a raised position to a lowered position.

The interior piston 116 has a lower engaging surface 128 that engages a flat head 126 of a rod 122, and the rod slidably extends into a suction aperture 124 formed in the handle's bottom portion 102. The rod 122 extends through a piston-biasing spring 130 that is positioned between the rod's flat head 126 a lower seat portion 132 formed in the handle's body portion 106. Accordingly, the piston-biasing spring

130 biases the rod 122 and the interior piston 116 away from the handle's bottom 102 portion, thereby pressing the plunger 114 toward the raised position.

A seal member 134 is provided at the upper end of the suction aperture 124, and the seal member sealably engages the rod 122. The seal member 134 prevents air within the suction aperture 124 from exiting through the suction aperture's upper end when the interior piston 116 presses the rod 122 into the suction aperture upon depression of the plunger 114. A connecting passageway 136 interconnects the suction aperture 124 with the interior channel 110 at the sensor-assembly receiving aperture 108 to allow the air to exit or enter the suction aperture.

Air is pushed out of and drawn into the suction aperture 124 by moving the rod 122 axially within the suction aperture, which is achieved by pumping the plunger 114 so as to axially move the interior piston 116 within the cylinder. Because the sensor-assembly receiving aperture 108 in the handle's bottom portion 102 communicates with the carrier-receiving portion 30 a significant suction will only be generated in the drawing tube 16 when the sensor-assembly receiving aperture 108 is fully sealed. When the sensor-assembly receiving aperture 108 is sealed, the only path for air to move into and out of the suction aperture is through the connecting channel 136 and the interior channel 110 within the drawing tube 16. As discussed in detail below, the wave-guide sensor assembly 10 is adapted to fully seal the sensor-assembly receiving aperture 108 to allow for accurate and controlled suction within the drawing tube when the plunger 114 is pumped.

As best seen in Figure 8, the carrier-receiving portion 30 removably receives the wave-guide sensor assembly 10 in an installed position. When the wave-guide sensor assembly 10 is in the installed position, the open bottom end 36 of the probe cover 32 is received in a recess 140 formed in the handle's bottom portion 102 around the sensor-assembly receiving aperture 108. The probe cover's open top end 34 is immediately adjacent to the handle's top portion 104 so the probe cover 32 is coaxially aligned with the sensor-assembly receiving aperture 108 and the drawing tube 16 in the handle's bottom portion 102. The carrier's coupling member 26 slides between the handle's top and bottom portions 104 and 102. Accordingly, the coupling member's

body portion 40 and sensor-receiving portion 44 are also coaxially aligned with the sensor-assembly receiving aperture 108 and the drawing tube 16.

When the coupling member 26 is in the sensor-retracted position, the sensor-receiving portion 44 is positioned within the probe cover 32 generally adjacent to the handle's top portion 104 and away from the sensor-assembly receiving aperture 108. A sensor 20 that is installed on the coupling member 26 is also positioned fully within the probe cover 32 and spaced away from the sensor-receiving aperture 108, so the sensor is protected from damage or contamination. When the coupling member 26 is in the sensor-extended position, the sensor-receiving portion 44 extends into the sensor-assembly receiving aperture 108. The probe 56 of the installed sensor 20 extends through the drawing tube 16 with the sensing area 28 exterior of the drawing tube and ready to engage the selected sample.

An O-ring seal 141 is mounted on the sensor receiving portion 44 and is positioned to sealably engage the walls of the sensor-assembly receiving aperture 108 when the coupling member 26 is in the sensor-extended position. The O-ring seal 141 blocks the passage of air through the upper end of the sensor-assembly receiving aperture 108 so the only passageway for air into and out of the suction aperture 124 is through the drawing tube 16. Therefore, the pipette 12 of the preferred embodiment creates drawing suction through the drawing tube 16 only when the wave-guide sensor assembly 10 is in the installed position and the coupling member 26 is in the sensor-extended position. The suction is created whether or not the sensor 20 is connected to the coupling member 26.

When a user depresses the plunger 114, the plunger moves the interior piston 116 downwardly thereby moving the rod 122 downwardly into the suction aperture 124, which forces air out of the suction aperture through the connecting channel 136. When the plunger 114 is released, the biasing spring 130 moves the rod 122 upwardly within the suction aperture 124, thereby creating suction within the suction aperture 124 that draws air from the drawing tube's interior channel 110, through the connecting channel 136, and into the suction aperture. The amount of suction created is controlled by regulating the stroke length or distance traveled by the rod 122 within the suction aperture 124 when the plunger 114 is depressed and released.

When the pipette tip 14 is retained on the drawing tube, placed into a sample, and plunger 114 is depressed and released, suction is generated within the pipette tip so as to draw the sample into the pipette tip. When the sensor 20 is connected to the coupling member 26, the sensor's sensing area 28 extends into the pipette tip 14. As the sample is drawn into the pipette tip 14, the sample is also drawn into engagement with the sensing area 28 for quick, easy, and accurate measurements.

In the preferred embodiment, the plunger 114 is connected to the interior piston 116 by a plunger shaft 138 that threadably receives the plunger 114. The stroke length of the rod 122 is controlled by adjusting the position of the plunger 114 on the plunger shaft 138. The further the plunger is screwed onto the plunger shaft 138, the shorter the stroke length of the rod 122, thereby resulting in less suction within the drawing tube 16.

As best seen in Figure 1, coupling member 26 is releasably located in the sensor-extended position when the wave-guide sensor assembly 10 is installed on the pipette 12. The body portion 106 of the pipette's handle 100 has a grip-receiving portion 142 adjacent to the carrier-receiving portion 30 and also adjacent to the handle's bottom portion 102. The grip-receiving portion 142 is positioned and sized to releasably receive the gripping portion 46 of the coupling member 26 in a locked position when the coupling member is in the sensor-extended position and the probe cover 32 rotated about its central axis toward the grip-receiving portion. The grip-receiving portion 142 has an upper endwall 143 that blocks the gripping portion 46 from sliding away from the handle's bottom portion 102 when in the locked position. Accordingly, the grip-receiving portion 142 provides a locking feature that releasably locks the coupling member 26 in the sensor-extended position to prevent inadvertent upward movement of the sensor 20 during a sampling procedure.

The gripping portion moves to an unlocked position when the probe cover 32 and coupling member 26 are rotated as a unit away from the grip-receiving portion 142. In the unlocked position, the gripping portion 46 is movable upwardly toward the handle's top portion 104 so as to slide the coupling member toward the sensor-retracted position.

In the preferred embodiment, the gripping portion 46 has a semicylindrical inner surface that extends around the probe cover 32. Edges of the gripping portion 46 are immediately adjacent to the edges of the handle's body portion 106 at the carrier-receiving portion 30, so rotation of the coupling member 26 and probe cover 32 is restricted by the edges of the handle's body portion. Accordingly, the coupling member 26 and probe cover 32 are rotatable relative to the pipette 12 only when the gripping portion 46 is positioned adjacent to the grip-receiving portion 142 or another grip-receiving area formed in the handle 100.

As best seen in Figures 1 and 8, the pipette 12 has a carrier-lock member 145 connected to the handle's top portion 104 and adapted to releasably lock the wave guide-sensor assembly 10 in the installed position. The carrier-lock member 145 includes a pair of biased retaining arms 144 that extend into the carrier-receiving portion 30 and releasably engage the open top end 34 of the probe cover 32 when the wave-guide sensor assembly 10 is in the installed position. The retaining arms 144 each have an engaging tab 146 that extends over the edge of the probe's open top end 34 and abuts the sidewall of the probe cover 32 so as to block the probe cover from inadvertently moving away from the handle 100 and out of the carrier-receiving portion 30.

The carrier-lock member 145 is moved to an unlocked position by sliding the coupling member 26 upwardly, past the sensor-retracted position and pressing the gripping portion 46 into engagement with the engaging tabs of the retaining arms 144. The gripping portion 46 moves the retaining arms 144 upwardly so the retaining tabs 146 are out of engagement with the probe cover 32. The probe cover 32 and the coupling member 26 are then moved as a unit away from the pipette's carrier-receiving portion 30. Accordingly, the wave-guide sensor assembly 10 is removed from the pipette 12 only when the coupling member 26 and the sensor 20, if installed, are in the sensor-retracted position.

The top portion 104 of the pipette's handle 100 has a U-shaped cable-receiving groove 148 that receives the fiber optic cable 22 therethrough when the wave-guide sensor assembly 10 is in the installed position. The cable-receiving groove 148 allows the fiber optic cable 22 to move with the coupling member 26 between the sensor-retracted and sensor-extended positions without binding or bending the fiber

optic cable past a predetermined minimum bend radius so as to maintain efficient propagation of the electromagnetic radiation through the fiber optic cable.

As best seen in Figures 8 and 9, the pipette 12 has a tip ejector 150 connected to the handle 100 that is adapted to eject the pipette tip 14 from the end of the drawing tube 16. The tip ejector 150 has an ejector tube 152 movably positioned adjacent to the pipette's drawing tube. The ejector tube 152 concentrically surrounds the drawing tube 16 and extends away from the handle's bottom portion 102 and terminates at an ejector surface 153. The ejector surface 153 is spaced apart from the end of the drawing tube 16 to allow the pipette tip 14 to extend over and releasably engage an exposed portion of the drawing tube. The pipette tip 14 terminates at a position adjacent to the ejector surface 153 when the tip ejector 150 is in a retracted, disengaged position, shown in Figure 8. The tip ejector 150 is movable to an extended, ejection position, shown in Figure 9, wherein the ejector surface 153 moves toward the end of the drawing tube 16, engages the pipette tip 14, and pushes the pipette tip off the drawing tube 16.

The tip ejector 150 has an ejector foot 154 that supports the ejector tube 152 and that is movably received within a recess in the handle's bottom portion 102. An ejector rod 156 is securely connected at its bottom end to the ejector foot 154 and extends upwardly through the handle's bottom portion 102, and terminates at an ejector head 158 positioned within the handle's body portion 106. The tip ejector 150 is biased toward the retracted, disengaged position by a biasing spring 159 that is slightly compressed between the bottom of the ejector head 158 and the handle's bottom portion 102. The ejector tube 152 is moved to the extended, ejection position to eject the pipette tip 14 when an ejection force is exerted on the ejector head 158 and the ejector rod 156 moves away from the handle's body portion 106, thereby causing the ejector foot 154 and the ejector tube to move relative to the drawing tube 16 to the extended, ejection position.

The tip ejector 150 includes an ejector piston 160 engaging the ejector head 158 and being slidably positioned within the handle's cylinder 120. The ejector piston 160 is positioned adjacent to the interior piston 116, and a movable activation blade 164 positioned to releasably engage the interior piston extends away from the

ejector piston. The activation blade 164 is slidably engaged by an activation pin 166 that extends through an aperture 168 in the handle's body portion 106 and partially into the carrier-receiving portion 30. The tip ejector 150 is activated by depressing the activation pin 166, as discussed in greater detail below, and then depressing the pipette's plunger 114, resulting in ejection of the pipette tip 14.

The activation blade 164 is movable between a disengaged position wherein it is out of engagement with the interior piston 116, illustrated in Figure 8, an activating position engages the interior piston. The activation blade 164 is biased toward the disengaged position, which presses the activation pin 166 partially into the carrier-receiving portion 30. When the activation blade 164 is in this disengaged position and the user depresses the plunger 11, the interior piston 116 does not engage the activation blade 164 as the interior piston moves toward the handle's lowered position. Accordingly, tip ejector 150 is not moved to the extended, ejection position and it remains in the retracted, disengaged position. When the activation pin 166 is pressed toward the interior piston 116, the activation blade 164 moves to the activating position and into engagement with the interior piston. Movement of the interior piston 116 toward the housing's bottom portion 102 causes the activation blade 164 and the ejector piston 160 to simultaneously move, thereby moving the ejector foot 154 and the ejector tube 152 to the extended, ejection position.

As best seen in Figures 8 and 9, movement of the activation pin 166 and the activation blade 164 relative to the interior piston 116 is controlled by the rotational position of the probe cover 32 when the wave-guide sensor assembly 10 is in the installed position. The probe cover 32 has an elongated ejector slot 168 positioned to receive the activation pin 166 when the coupling member 26 is in the sensor-retracted position and the sensor-extended position. As the coupling member 26 slides between the sensor-retracted position and the sensor-extended position, the activation pin 166 remains protruding through the ejector slot 168 so the tip ejector 150 will not move as the user depresses the plunger 114. The ejector slot 168 is also sized to receive the activation pin 166 when the probe cover 32 and coupling member 26 are rotated relative to the pipette 12, when the coupling member 26 is in the sensor-extended position, to the locked position.

The probe cover 32 and the coupling member 26 are also rotatable relative to the pipette 12 in the opposite direction when in the intermediate position. However, the activation pin 166 does not remain in the ejector slot 158, so the activation pin is pressed toward the interior piston 116, thereby moving the activation blade 164 into engagement with the interior piston for activation of the tip ejector by the user upon depressing the plunger 114. As best seen in Figure 1, the housing's body portion 106 has an intermediate grip-receiving portion 170 formed therein at a position corresponding to the intermediate position of the coupling member 26. The intermediate grip-receiving portion 170 is adjacent to the carrier-receiving portion 30 and on the opposite side from the lower grip-receiving portion 142. In the intermediate position, the sensor's sensing area 28 is contained and protected within the drawing tube 16.

When the coupling member 26 is in this intermediate position, shown in Figure 9, the probe cover 32 and coupling member 26 are rotatable as a unit so the gripping portion 46 moves into the intermediate grip-receiving portion 170. As the probe cover 32 rotates toward the intermediate grip-receiving portion 170, the probe cover's ejector slot 168 is rotated away from the activation pin 166 thereby causing the exterior surface of the probe cover 32 to press the activation pin 166 inwardly toward the interior piston 116, which moves the activation blade 164 into engagement with the interior piston 116. The tip ejector 150 is then ready to eject the pipette tip 14 upon depressing the plunger 114.

In the preferred embodiment, the activation blade 164 moves into engagement with the interior piston 116 for activation of the tip ejector 150 only when the interior piston 116 is in the raised position, when the coupling member 26 is in the intermediate position, and when the gripping portion 46 rotated into the intermediate grip-receiving portion 170. As the probe cover 32 presses the activation pin 166 inwardly, the activation blade 164 is moved into engagement with the interior piston 116, as shown in Figure 9, and the tip ejector 150 ejects the pipette tip 14 upon depressing the plunger 114.

The plunger 114 presses the interior piston 116, the activation blade 164, and the ejector piston 160 downwardly, which moves the ejector rod 156, the ejector foot 154, and the ejector tube 150 to the extended, ejection position and pushes the

pipette tip 14 off of the drawing tube 16. Accordingly, the user can eject the pipette tip 14 into a suitable waste receptacle after sampling a selected sample without the user ever having to touch the pipette tip and risking contamination of the user's hand or the equipment used during the sampling procedure. A new pipette tip 14 is then attached to the drawing tube 16, the sensor 20 is then moved to the sensor-extended position, a sample is drawn into the new pipette tip 14 and into engagement with the sensor's sensing end 28.

If an initial analysis of a sample is not sufficiently complete, the sensor 20 can also be withdrawn from the pipette tip 14, moved to the intermediate position, and then reintroduced into the pipette tip 14 for additional analysis. If the sample does not need further analysis, the pipette tip 14 is ejected when the sensor 20 is in the intermediate position, a new pipette tip is installed on the pipette drawing tube, and the sensor is moved to the sensor-extended position. Another sample is drawn into the pipette tip 14 and is analyzed as the sample contacts the sensor's sensing area 28. After the sample has been analyzed, the sensor 20 is moved to the sensor-retracted position or the intermediate position to cover and protect the sensing area 28 from being inadvertently impacted, contaminated, or otherwise damaged.

In the preferred embodiment, the pipette tip 14 that is used with the pipette 12 and the wave-guide sensor assembly 10 has a generally conical-shaped sidewall that defines an open top end sized to partially fit over the drawing tube 16 and an open bottom end with a small opening through which the selected sample is drawn into the pipette tip.

In another embodiment, the same embodiment above is used where the pipette tip's sidewall also defines an interior surface that communicates with the selected sample drawn into the pipette tip. The pipette tip's interior surface is coated with a selected chemical treatment that is utilized during a sampling procedure. The selected chemical treatment, forming a surface coating on the inside wall of the pipette tip 14, provides a means for preparation of a specific surface for solid-phase reaction, for biologically active surfaces, for surfaces preactivated for subsequent coupling reactions, or for further functionalization or derivatization. The selected chemical treatment can be a duplicate of the chemistry on the sensor tip or may optionally be an alternative

chemistry, depending on the application. The surface coating of one embodiment provides an additional surface area to extend the binding capacity and thus separation of selective chemical or biochemical agents from the bulk solution contained in the pipette tip 14. The selected surface coating also allows the pipette tip 14 to be used in containing, concentrating, purifying and/or transporting selective chemical or biochemical agents, such as for use in other chemical/biochemical processing (i.e., further purification, PCR, further interaction analysis studies) or chemical analysis (i.e., mass spectrometry, etc.)

Use of the sensor 20 and pipette tip 14 with the selected surface coating for direct analysis and simultaneous handling of the agent for processing, as discussed above, results in the advantages of time savings, qualities in results, etc. For example, in such an application, the selective chemistry on the sensor tip and the modified inside wall of the pipette tip 14 can bind a specific chemistry on the sensor tip and the modified inside wall of the pipette tip can bind a specific chemical agent, the sensor response thus confirming the specificity. The agent may then, under selected chemical conditions, be washed off from the pipette tip wall and the sensor into a container for further processing.

In one embodiment, the pipette tip is a finned-pipette tip that has a plurality of fins extending radially inwardly from the sidewall toward the axis of the pipette tip. The fins provide an increased surface area within the pipette tip that is available to contact the selected sample. These fins are also coated with the selected chemical treatment so the surface area of the chemical treatment within the finned-pipette tip that is available to contact the selected sample is greater than the available surface area of a non-finned pipette tip. In other embodiments, the increased surface area in the pipette tip is provided by a hydrogel layer or a layer of small porous particles that are chosen for use with selected sensors in selected sampling processes.

In one embodiment, the sample drawn into the pipette tip is agitated or stirred to provide movement of the sample relative to the probe's sensing area. Such movement or hydrodynamic agitation of the sample provides an increased mass transport of the chemical or biochemical species in the sample to the sensor area achieving accurate measurements and avoiding static conditions. Such movement or

hydrodynamic agitation of the sample in the pipette tip 14 may be achieved by providing a piezoelectric stirrer or other mixing devices that cycle into and out of the pipette tip. Movement may also be achieved by moving or vibrating the probe 56 when it is extended into the pipette tip 14 and into the sample.

Difficulties in mass transport in some testing procedures may be associated with static hydrodynamic conditions within the pipette tip 14. Such mass transport difficulties may be overcome by oscillating the sample level within the pipette tip 14. As best seen in Figure 10, an alternate embodiment of the present invention includes a drawing mechanism 300 that is operatively coupled to the pipette's drawing tube 16 to create selected negative and positive pressures within the drawing tube's interior passageway 110 and in the pipette tip 14 when the pipette tip is installed. Negative pressure is used to draw a sample into the pipette tip 14, and the pressure is then oscillated between selected positive and negative pressures to axially oscillate the sample within the pipette tip. The drawing mechanism 300 in one embodiment is an automated drawing mechanism that is used in lieu of the manual drawing mechanism 112 (Figure 8) described earlier. The automated drawing mechanism 300 preferably includes a conventional reciprocating pump consisting of a piston within a cylinder, wherein the piston has specific static positions, as well as different frequencies and stroke amplitudes. In this configuration, the volume of air or other gas introduced and expelled from the drawing mechanism 300 is highly controlled by controlling the frequency and stroke amplitude, thereby allowing for highly controlled oscillation of the sample within the pipette tip 14.

The drawing mechanism 300 is operatively connected to the pipette 12 by a hydraulic or pneumatic tube 302. One end 301 of the tube 302 is connected to a tube connector 304 on the bottom portion 102 of the pipette handle. The tube connector 304 has an air passageway 305 that communicates with the suction aperture 124 in the pipette handle's bottom portion 102. The connecting passageway 136 in the bottom portion 102 interconnects the suction aperture 124 with the drawing tube's interior channel 110 at the sensor-assembly receiving aperture 108 to allow air or other selected gas, such as nitrogen, to exit or enter the drawing tube's interior channel and the pipette tip 14. When the wave-guide sensor assembly 10 is in the installed position, the drawing

mechanism 300 generates the alternating positive and negative pressure in the pneumatic tube 302, the tube connector 304, the suction aperture 124, the connecting passageway 136, and the drawing tube 16, thereby causing oscillating pressures within the drawing tube and the pipette tip 14. Accordingly, the alternating pressures cause the sample level within the pipette tip 14 to rise and fall in a controlled and oscillatory manner.

In operation, the drawing mechanism 300 generates a negative pressure in the pipette tip 14 while the pipette tip is inserted into a sample, thereby drawing a selected volume of the sample into the pipette tip. As best seen in Figure 11, the sample's upper level within pipette tip 14 after the sample is first taken is at an initial upper position AH, and the sample's lower level is at a lower position AL at the lower end of the pipette tip. When the fiber optic probe 56 is in the sensor-extended position with the sensing area 28 in the sample, the drawing mechanism 300 is activated and generates the alternate positive and negative pressures within the pipette tip 14.

When the drawing mechanism 300 generates the negative pressure during a suction phase, the sample's upper and lower levels move axially relative to the probe's sensing area 28 toward the pipette's drawing tip 16 to raised upper and lower positions CH and CL, respectively, shown in phantom lines. When the drawing mechanism 300 generates the positive pressure during a pressure phase, the sample is moved axially away from the drawing tip 16 so the sample's upper level moves from the raised upper level CH to a lowered upper level BH, shown in phantom lines. The sample's lower level moves from the raised lower level CL to the end of the pipette tip 14. If the positive pressure is sufficient, a small amount of the sample is expelled from the pipette tip during the pressure phase. The sample's oscillatory movement within the pipette tip 14 relative to the probe's sensing area 28 causes a forced convective flow around the sensing area, thereby counteracting the creation of a concentration gradient within the sample.

As best seen in Figure 12, an alternate embodiment includes the pneumatic tube 302 that extends through the pipette handle 100 and connects to an air passageway 350 in the handle's bottom portion 102. The air passageway 350 communicates with the suction aperture 124 and is positioned above the connecting channel 136. Accordingly, the air passageway 350 is coupled to the drawing tube's

interior passageway 110 via the suction aperture 124 and the connecting channel 136. In another alternate embodiment, the pneumatic tube 302 is positioned along the exterior of the pipette handle's main body portion 106 and connects to a connection port 351 in the handle's bottom portion 102. The connection port 351 is connected to the air passageway 350 so as to operatively connect the pneumatic tube 302 to the air passageway. In each of these alternate embodiments, the pneumatic tube 302 is operatively coupled to the drawing tube's interior channel 110, and thus to the interior of the pipette tip 14, so as to allow the positive and negative pressures to be transmitted to the pipette tip for sample oscillation relative to the sensing area 28.

As best seen in Figure 13, an alternate embodiment of the present invention includes a pipette tip 14 that is partially constricted at a position below the pipette's drawing tube 16. The partially constricted pipette tip has a lower portion 14a, a constricted middle portion 14b, and an upper portion 14c. The constricted middle portion 14b is generally adjacent to the sensing area 28 when the probe 56 is in the sensor-extended position, and has a cross-sectional area that is smaller than the cross-sectional areas of the lower portion 14a and the upper portion 14c. The constricted middle portion 14b has a length that substantially corresponds to the length of the probe's sensing area 28, and the middle portion is positioned to contain substantially all of the sensing area when the probe is in the sensor-extended position. As such, the pipette tip 14 behaves as a venturi, so the sample flow rate within the pipette tip 14 during sample oscillation increases as the sample moves through the constricted middle portion 14b. The increased flow rate of sample next to the probe's sensing area 28 significantly reduces drawbacks related to mass transport.

As best seen in Figure 14, an alternate embodiment of the partially constricted pipette tip has an elongated constricted middle portion 14b extending between the upper and lower tip portions 14c and 14a. The elongated middle portion 14b is adapted for use with a sensor having an elongated sensing area 28, so substantially all of the sensing area is positioned within the constricted middle portion when in the sensor-extended position. In this alternate embodiment, the lower tip portion 14a is also removably connected to the middle portion 14b. The lower tip portion 14a is preferably

attached to the middle portion 14b by a friction fit therebetween, such that the lower portion can be removed and replaced during selected procedures.

As best seen in Figures 15 and 16, another alternate embodiment of the pipette tip 14 includes upper and lower tip portions 14d and 14e. The upper tip portion 14d removably attaches to the pipette's drawing tube 16, and the lower tip portion 14e is removably attached to the upper tip portion. The lower tip portion 14e of the illustrated embodiment is an elongated portion defining a micro-pipette tip that is adapted to retain samples in very low volumes ranging from 2 to 20 microliters (*i.e.*, 2-20 µl), inclusive. In the alternate embodiment as shown in Figure 16, the lower tip portion 14e defines a micropipette tip that is shorter than the lower tip portion shown in Figure 15a, and is also sized to sample the low volumes ranging from 2-20 µl, inclusive. The different lower tip portions 14d and 14e are selected for use with samples of different viscosities so as to achieve optimum performance during a sampling procedure. For example, the longer lower tip portion 14e is used with low viscosity fluids to achieve the benefit of the capillary effect within the elongated tip portion. The shorter tip portion 14e is usable with samples having higher viscosity.

As best seen in Figures 17-19, an alternate embodiment includes a pipette tip 414 that provides a tip configuration adapted to move the probe's sensor area 28 laterally within the pipette tip when in the sensor-extended position and when the sample is oscillated axially within the pipette tip. The pipette tip 414 of this alternate embodiment has a generally oval cross-sectional shape with an interior area 320 having a generally elongated "S" or "Z" shape. The interior area 320 is defined by a lower shoulder portion 322 of the pipette tip 414 that is laterally and axially offset from an upper shoulder portion 324. The lower shoulder portion 322 extends upwardly from the pipette tip's lower end and terminates at an upper surface 326 located at the interior area's mid-portion 330. The upper shoulder portion 324 is spaced upwardly apart and laterally offset from the lower shoulder portion 322 so the upper and lower shoulder portions are on opposite sides of the pipette tip's longitudinal axis. The upper shoulder portion 324 has a lower deflecting surface 332 that is angled to deflect the sample flow laterally as the sample is oscillated within the pipette tip 414.

When the pipette tip 414 is on the drawing tube 16 and before sample is drawn into the pipette tip, the sensor area 28 is in a first lateral position in the pipette tip's interior area and is substantially coaxially aligned with the pipette tip's longitudinal axis, as shown in Figure 18. When sample is drawn into the pipette tip 414, the sample flow moves upwardly through the pipette tip adjacent to the lower shoulder portion 322, and to the upper shoulder portion's deflecting surface 332. The deflecting surface 332 deflects the sample flow laterally and into the pipette tip's upper portion. This lateral movement of the sample moves the probe's sensor area 28 laterally within the pipette tip to a second lateral position, shown in Figure 17, and shown in Figure 19 in phantom lines. In this second lateral position the sensor area 28 is off-set from the pipette tip's longitudinal axis and is immediately above the lower shoulder portion's upper surface 326. As the sample is oscillated in the pipette tip 14, the sample moves along the interior area's "S" or "Z"-shaped path, thereby waggling the probe's sensor area 28 laterally in the direction of arrows F1 (Figure 17) and F2 (Figure 18) between the first and second lateral positions. The probe's lateral movement in conjunction with the oscillatory, axial sample movement provides increased relative movement between the probe's sensing area 28 and the sample, thereby minimizing mass transport problems during a sampling and testing process.

In the embodiment illustrated in Figures 1, 8, and 9, the coupling member 26 is optically coupled to a remote fiber optic spectrograph 24 (Figure 1) by the fiber optic cable 22. In an alternate embodiment of the present invention shown in Figure 15, the hand-held pipette 12 has an internal detection and analyzing device 207 such as a fiber optic spectrograph contained within a housing portion 202 attached to the pipette's handle 100. The housing portion 202 also contains a light or electromagnetic radiation source 204, a self-contained power source 206 such as a battery, and a microprocessor 205, coupled to the power source. A wave guide cable 208 optically couples the electromagnetic radiation source 204 and the detection and analyzing device 207 to the coupling member 26 of the wave-guide sensor assembly 10. The wave guide cable 208 has a sufficient length that allows the coupling member 26 to move between the sensor-retracted position and the sensor-extended position. The connecting portion 202 is adapted for receiving a portion of the wave guide cable 208 therethrough when the

coupling member is in the sensor and retracted position. Accordingly, this self-contained, hand-held pipette 12 and internal fiber optic spectrograph 200 can be carried to remote locations without concern for connection to remotely located fiber optic spectrographs, detection and analyzing devices and power sources.

In another alternate embodiment illustrated in Figure 20, a display module 210 is mounted to the pipette handle 100 and operatively coupled to the fiber optic spectrograph. The display module 210 is adapted to receive sampling results from the fiber optic spectrograph and to display the results at a location that allows a user to read the sampling results during or immediately after the sampling procedure. In one alternate embodiment, the display module is a digital display operatively coupled to the detection device 207 of the internal fiber optic spectrograph 200 on the hand-held pipette.

In an alternate embodiment of the invention shown in Figure 21, the pipette 12 includes a regulator 360 positioned in the pipette handle's bottom portion 102 and within the suction aperture 124. The regulator 360 is adapted to control the amplitude of the sample oscillation in the pipette tip by controlling the amount of air or other gas that is moved within the pipette tip 14 during the suction and pressure phases.

The regulator 360 of the exemplary embodiment is positioned in the suction aperture 124 between the air passageway 305 of the tube connector 304 and the connecting channel 136. The regulator 360 includes an upper stop 362, a lower stop 364 spaced apart from the upper stop, and a piston 366 slidably retained in the suction aperture 124 between the upper and lower stops. The piston 366 slides between the upper and lower stops 362 and 364 during the pressure and suction phases. During the pressure phase, a positive pressure is transmitted through the tube connector 304 into the suction aperture 124 above the piston 366. This positive pressure pushes the piston downwardly in the suction aperture 124 to the lower stop 364. Accordingly, the piston 366 causes movement of a selected volume of air or other gas within the connecting channel 136, the drawing tube's interior channel 110, and the pipette tip 14, thereby moving the sample to the lower position.

During the suction phase, a negative pressure is generated in the suction aperture 124 above the piston 366, and the piston is drawn upwardly from the lower

stop 364 to the upper stop 362. Accordingly, the piston 366 movement causes a selected volume of air or other gas to be drawn from the pipette tip above the sample, thereby drawing the sample within the pipette tip 14 upwardly toward the drawing tube 16.

In the exemplary embodiment shown in Figure 21, the lower stop 364 is axially adjustable to increase or decrease the piston's stroke length. The lower stop 364 is connected to an actuator rod 367 that extends through an aperture in the pipette handle's bottom portion 102. The actuator rod 367 is connected to an adjustable stop driver 368 that is adapted to selectively move the actuator rod axially, thereby moving the lower stop 364 to a selected position. The position of the lower stop 364 in the suction aperture 124 is selected to control the amplitude of the sample's oscillation in the pipette tip 14. In one alternate embodiment, the lower stop's position is initially selected to control the amount of the sample initially drawn into the pipette tip 14. The lower stop 364 is then adjusted to shorten the piston's stroke length so as to provide the desired sample oscillation during a sampling procedure without ejecting all of the sample from the pipette tip. Accordingly, the regulator 360 is adjustable to control the sample volume and the sample's oscillation amplitude in the pipette tip 14.

As best seen in Figure 22, the lower stop 364 in another alternate embodiment is connected to a rack and pinion positioning assembly 380. The positioning assembly 380 controls the lower stop's axial position within the suction aperture 124. The positioning assembly 380 includes an actuator 382 that extends through an aperture in the pipette handle's bottom portion 102. The actuator rod 382 has a distal portion with a plurality of teeth 384 thereon that defines a rack 385. The rack 385 is connected to a pinion 386 of a stop positioner 388, which is mounted to the pipette handle's bottom portion 102. The stop positioner 388 rotates the pinion 386 on the rack 385, thereby axially moving the actuator rod and the lower stop 364 to a selected position in the suction aperture 124.

In the exemplary embodiment illustrated in Figure 22, the piston 366 is biased toward the upper stop 362 by a spring 390 or other biasing member positioned in the suction aperture 124. The illustrated spring 390 is a coil spring, and the lower stop 364 is positioned within the coil spring. As the piston 366 is moved axially toward the

lower stop 364, the piston compresses the spring 390 until the piston reaches the lower stop. The spring 390 then returns the piston to a position adjacent to the upper stop 362, wherein the piston is ready for the next piston stroke.

As best seen in Figure 23, an alternate embodiment of the present invention includes a bellows regulator 370 that is operatively connected to the pneumatic tube and positioned partially within the suction aperture 124. The bellows regulator 370 is connected to a distal end portion 372 of the rod 122, which is axially movable in the suction aperture 124. The rod's distal end portion 372 has an air channel 374 therein that is connected to the pneumatic tube 302, so air or other selected gas from the tube is carried to the rod's distal end portion.

The bellows regulator 370 has an expandable bellows 376 connected to the rod's distal end portion 372 and positioned in the suction aperture 124. The bellows 376 axially expands and contracts in the suction aperture 124 during the pressure and suction phases so as to cause the sample oscillation in the pipette tip 14. The length of the bellow's axial expansion and contraction is controlled by the volume of air or other gas, or suitable liquid, moved through the hydraulic or pneumatic tube 302 during the pressure and suction phases. Accordingly, the length of axial expansion and contraction controls the positive and negative pressure generated in the pipette tip 14, thereby controlling the amplitude of the sample oscillation.

The embodiments of the present invention discussed above have been discussed primarily in connection with the use of a fiber optic probe. Alternate embodiments, however, include other sensors, such as electrochemical sensors, surface acoustic sensors, transmission absorption sensors, or the like. An alternate embodiment of the present invention, illustrated in Figure 25, has an electrochemical sensor 400 connected to the coupling member's sensor receiving member. The sensor's distal end includes an electronic conductor 402 and a pair of electrodes 404 adjacent to the conductor. The sensor's distal end is adapted to extend into the pipette tip 14 during the sample oscillation as discussed above.

The sensor's proximal end has a connector 406 that is operatively connected to an electronic cable 408. The electronic cable 408 is connected at one end to the sensor carrier 18 so as to retain the cable in a substantially fixed position relative

to the sensor 400 when the sensor is installed. The cable's opposite end (not shown) is coupled to a selected analyzer or other testing device for testing of the sample.

As best seen in Figures 22 and 24, an alternate embodiment of the invention includes a quick release sensor assembly 420 adapted to be releasably connected to the sensor carrier 18. The sensor assembly 420 includes an elongated housing 422 that contains the sensor 56. The proximal end of the housing 422 has a connection portion 424 that is received and releasably retained by the sensor carrier 18 so as to operatively connect the sensor 56 to the cable. In one embodiment, the sensor 56 is a fiber optic sensor, and the connection 402 is shaped and sized to axially align and optically couple the sensor to the fiber optic cable 22.

The connection portion 424 of the illustrated embodiment has an annular receiving area 426 that receives retaining pins 428 (Figure 22) in the lower body portion 102 of the pipette or other sampling device. The retaining pins 428 are movable between an engaged position with the pins being within the annular receiving area 426 and a released position, shown in phantom lines, with the pins being exterior of the annular receiving area. In the engaged position, the sensor assembly 420 is securely retained in the sensor carrier 18. In the released position, the sensor assembly 420 may be removed from or installed into the sensor carrier 18, and the pins are then moved to the engaged position.

The distal end portion of the housing 422 contains the sensor's sensing area 28. The sensing area 28 is space apart from housing by a space defining a flow channel 430 around the sensing area. The distal end of housing 422 is open so sample can flow into the flow channel 430. The housing 422 also includes apertures 432 at the top of the flow channel 430 that allow the sample to flow into and out of the flow channel, particularly during sample oscillation. As best seen in Figure 22, the housing's open distal end is adapted to engage and sealably engage the pipette tip 14 when installed so sample drawn into the pipette tip flows into the housing's flow channel 430 around the sensing area 28 and out of the apertures 432. Accordingly, the sensing area 28 is protected by the housing 422 while being exposed to the sample flow during the sampling procedure.

The sensor assembly 420 is particularly well suited for use with automated testing equipment. As an example, one embodiment of the invention includes an automated process of inserting the sensor assembly 420 into a pipette or other suitable sampling device when the retaining pins are in the released position, and then moving the retaining pins to the engaged position. A pipette tip 14 is then installed on the pipette's drawing tube 16 and the pipette and pipette tip are moved as a unit to a sample position wherein a selected sample is drawn into and oscillated within the pipette tip for analyzing the sample. After the sample is analyzed, it is ejected from the pipette tip, the pipette tip is ejected and the sensor assembly 420 is prepared for analyzing another selected sample. In the automated embodiment, a plurality of pipettes and sensor assemblies 420 can be used to simultaneously test or analyze a plurality of samples.

As best seen in Figure 26, another alternate embodiment of the present invention includes the wave-guide sensor assembly 10 mounted on a stand 220 used during testing of selected samples. The stand 220 has a connecting arm 222 that removably receives the wave-guide sensor assembly 10, and the connecting arm is movably mounted to a shaft 224 projecting upwardly from a base 226. The connecting arm 222 is movable with the wave-guide sensor assembly 10 relative to the base 226 between a lowered, sensing position and a raised, ready position.

The connecting arm 200 is attached to a tubular support member 228, which securely holds the coupling member 26 at a fixed location relative to the connecting arm. The probe cover 32 is concentrically mounted around the tubular support 228 and is axially movable relative to the coupling member 26 and the sensor 20 mounted thereto between a raised, sensor-exposed position to expose the sensor's sensing area 28, and a lowered, sensor position to cover and protect the sensor 20.

During a sampling procedure, the probe cover 32 is maintained in the lowered sensor-retracted position with the sensor 20 fully contained until a selected sample is ready to receive the probe's sensing area 28. The probe cover 32 is slid upwardly to the raised, sensor-exposed position, thereby exposing the sensing area 28. The wave-guide sensor assembly 10 and the stand's support arm 222 are moved downwardly as a unit relative to the stand's base 226 and the probe's sensing area 28 is

dipped into the selected sample. After completion of the sampling, the support arm 222 and wave-guide sensor assembly 10 are moved upwardly to a raised position, and the probe cover 32 is moved over the sensor 20 to the lowered, sensor-retracted position.

As best seen in Figure 27, an alternate embodiment of the invention includes a sensor assembly 450 mounted on an adjustable stand 452 that is moveable along the X, Y, and Z axes. The sensor assembly 450 includes a sensor carrier 454 mounted to an arm 456 of the stand 452. The sensor carrier 454 includes a probe cover 458 that slidably retains a sensor coupling member 460, similar to the sensor assembly discussed above in connection with the pipette. The coupling member 460 is attached to the fiber optic cable 22 and is adapted to removably receive the sensor 56 therein.

As best seen in Figure 28, the sensor carrier's bottom portion 462 is attached to a base assembly 464 that is substantially similar to bottom portion of the pipette handle discussed above. A tip ejector 150 is attached to the bottom portion 462 for ejection of the pipette tip 14 from the drawing tube 16. The bottom portion 462 also includes a sensor receiving aperture 108 that is coaxially aligned with the drawing tube 16. An air passageway 466 extends through the bottom portion 462 and communicates with the receiving aperture 108 and the drawing tube's interior area 110. A pneumatic tube 470 is connected to the other end of the air passageway 466 so air or other gas can be used to create positive and negative pressures in the pipette tip 14 for oscillation of the sample therein, as discussed above. In the illustrated embodiment, the tube 470 is removable connected to the bottom portion 462 and an O-ring seal 472 is positioned between the tube and the bottom portion to maintain a substantially air-tight seal therebetween.

In an another alternate embodiment of the invention shown in Figure 29, a plurality of the stand-mounted sensor assemblies 450 are mounted to a support structure 474, such as a stand assembly of an automated sampling device. The plurality of sensor assemblies 450 retain the sensors 56 therein. The support structure 474 includes a plurality of drawing tubes 16 that are positioned to removably receive pipette tips 14 thereon in a position to receive the sensors 56 when the sensors are in the sensor-extended position, as discussed above. Accordingly, the plurality of sensor assemblies 450 are usable simultaneously to test or analyze a plurality of samples.

Referring to Figures 30A-F, an alternate embodiment of the pipette 12 is illustrated. This alternate embodiment is similar to the pipette discussed above, and it has an elongated handle 100, an ergonomically-shaped thumb-activated plunger 114 and a retaining hook 115 adjacent to the plunger. The retaining hook 115 allows the pipette 12 to be hung on a retaining stand, or the like, such as during a long sampling procedure or when the pipette is not being used.

Experimental Examples

In order to better demonstrate the advantages of the present invention, several experiments were conducted. The results of these experiments are shown in Figure 31 and Figures 32A-C. The materials employed in these experiments included a Biacore probe instrument apparatus for surface plasmon resonance (SPR) detection, Sensor Probes CM5 for SPR, HBS buffer as a reference solution, and an amine coupling kit containing NHS, EDC, and ethanolamine (commercially available products from Biacore AB, Uppsala, Sweden), as well as sodium hydroxide TITRISOL (commercially available from Merck, Darmstadt, Germany). In addition, a prototype of the present invention, amino-H1 hapten, and monoclonal antibody were internally produced for purposes of experimentation.

Initially, a high-capacity ligand sensor surface was prepared by coupling a small molecule, amino-H1 hapten, to the carboxy methylated dextrane on the sensor probe. The carboxy-groups of the carboxy methylated dextrane were activated by a mixture of N-ethyl-N'-(dimethyl-aminopropyl) carbodiimide hydrochloride (EDC), and N-hydroxysuccinimide (NHS), both prepared in water. A solution of an amino derivative of a small molecule, hapten H1, was coupled to the activated groups on the sensor surface. Residual NHS-esters remaining after the ligand immobilization were then reacted with a solution of ethanolamine. Each of the three steps in this immobilization took 15 minutes and were performed at room temperature, 20°C.

The sample used was a monoclonal mouse antibody (Mab 515) directed against the H1 hapten. The concentration of the antibody was 1 or 0.3 μg/ml diluted in HBS buffer. The interaction time for the antibody sample with the sensor surface was three and five minutes, respectively. The sensor probe was reused a number of times by

regenerating it with 0.1 M sodium hydroxide and one minute of interaction. All of the experiments were performed at room temperature, 20°C.

The general method used in the experiments were as follows: (1) draw reference solution (HBS); (2) read measured SPR-response of reference; (3) dispense HBS; (4) aspirate sample; (5) dispense sample; (6) aspirate HBS; (7) dispense HBS; (8) aspirate HBS; (9) read measured SPR-response for sample interaction; and (10) regenerate sensor.

Referring now to Figure 31 and Figures 32A-C, experimental data is illustrated for a hand-held pipette with a fiber optic SPR sensor in accordance with an embodiment of the invention as shown in Figures 10 and 11. Specifically, Figure 31 compares the measured SPR-response of a non-oscillated sample, "A," with the SPR-response of an oscillated sample, "B." Here, sample Mab 515 (concentration 1 μg/ml) was manually drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. As shown, the sensor response increased approximately three-fold when the sample was oscillated.

Figures 32A-C compare the measured SPR-response of a non-oscillated sample with the SPR-response of an oscillated sample within a constricted pipette tip in accordance with the embodiment of the invention as shown in Figure 13. More specifically, Figure 32A demonstrates the influence that a sample's oscillation frequency and amplitude have on the measured SPR-response. Here, sample Mab 515 (concentration 1 μg/ml) was manually drawn into the constricted pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. As shown, the sensor response increased as the frequency and amplitude of sample oscillation was increased. In Figure 32A, "A" shows the SPR-response with no oscillation; "B" shows the SPR-response with low frequency and small amplitude of oscillation; and "C" shows the SPR-response with high frequency and small amplitude of oscillation; and "D" shows the SPR-response with high frequency and large amplitude of oscillation. These results indicate that as the frequency of oscillated forced convention is increased, the sensor response is also increased.

Figure 32B demonstrates the influence that the pipette tip (flow cell) geometry has on the measured SPR-response. Here, sample Mab 515 (concentration 1

μg/ml) was drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for three minutes. In Figure 32B, "A" shows the SPR-response of an oscillated sample within a pipette tip, whereas "B" shows the SPR-response of an oscillated sample within a constricted pipette tip. These results illustrate the improved flow dynamics within the constricted tip.

Figure 32C compares the measured SPR-response of a non-oscillated sample within a Gilson pipette tip with an oscillated sample and an oscillate reference solution, both of which were within a constricted pipette tip. Here, sample Mab 515 (concentration 0.3 μg/ml) was manually drawn into the pipette tip and allowed to interact with H1 antigen immobilized on the sensor surface for five minutes. In Figure 32C, "A" shows the SPR-response of a non-oscillated sample within a pipette tip; "B" shows the SPR-response of an oscillated sample within a constricted pipette; and "C" shows the SPR-response of an oscillated reference solution (HBS buffer) within a constricted pipette tip. These results also demonstrate the improved sensor response at oscillating forced sample convections.

Although specific embodiments of, and examples for, the present invention have been described above for purposes of illustration, various modifications can be made without departing from the spirit and scope of the invention, as will be evident by those skilled in the relevant art. For example, the sensor assembly 10 may be removably mounted to a tubular pipette adapter that removably receives the drawing tube of a conventional pipette and that provides an adapter drawing tube which coaxially aligns with the sensor assembly for drawing of the selected sample. Such a retrofit or adapter for a conventional pipette provides many benefits achieved by the exemplary embodiments discussed above and illustrated in the drawings. The teachings provided herein of the present invention can be applied to other sensor assemblies and other sampling devices, not necessarily those limited to hand-held, manually activated sampling devices. As an example, the pipette 12 or other sampling device can be provided with a motorized pumping mechanism adapted to create the selected partial vacuum at the drawing tube as is provided by the manual drawing mechanism described above.

Furthermore, while the present invention is generally described as being applied to pipettes and fiber optic sensors, the principles of the present invention can be

applied to other sampling devices and sensor systems. Accordingly, the invention is not limited by the disclosure, but instead its scope is to be determined entirely from the following claims.

CLAIMS

We claim:

1. A sensor assembly for use with a signal source and a signal carrying member connected to the signal source, comprising:

a sensor having a probe, the probe having a first end portion, a second alignment end portion, and a sensing area, the sensing area being a probe area at which the signal is generated or passed through; and

a sensor carrier having a receiving member attachable to the signal carrying member and attachable to the sensor, the receiving member being shaped to align the second alignment end portion of the probe with the signal carrying member for propagating a signal from the signal carrying member to the probe at the second alignment end portion.

2. The sensor assembly of claim 1 wherein the sensor is a wave-guide sensor, the probe is a wave-guide probe, the sensor carrier is a wave-guide sensor carrier, and the receiving member is a wave-guide receiving member, the wave-guide receiving member being shaped to align the second alignment end portion of the wave-guide probe with a wave-guide cable that is the signal carrying member for propagating electromagnetic radiation into the wave-guide probe.

3. The sensor assembly of claims 1 or 2, further comprising:

a pipette retaining the sensor carrier in an installed position.

4. The sensor assembly of claim 3, further including a drawing mechanism connected to the pipette and a pipette tip removably connected to the pipette and positioned to receive a portion of the probe therein, the drawing mechanism being operatively coupled to the pipette tip to generate a selected negative pressures in the pipette tip to allow a selected volume of a liquid sample to be moved within the pipette tip relative to the position of the probe.

5. The sensor assembly of claim 4 wherein the drawing mechanism is a sample handling mechanism operatively coupled to the pipette tip to generate selected positive and negative pressures in the pipette tip to allow a selected volume of a liquid sample to be moved within the pipette tip relative to the position of the probe.

6. The sensor assembly of claim 3, 4 or 5 wherein the sensor carrier is removably attached to the pipette and movable between an installed position with the sensor carrier in engagement with the pipette and a removed position with the sensor carrier being out of engagement with the pipette.

7. The sensor assembly of claim 6 wherein the pipette includes a locking mechanism releasably attached to the sensor carrier when the sensor carrier is in the installed position.

8. The sensor assembly of claim 3, 4, or 5 wherein the pipette has a a tip receiving portion coupled to the drawing mechanism, and a tip ejector connected to the drawing mechanism and positioned adjacent to the tip receiving portion, the tip receiving portion being shaped to releasably receive a pipette tip thereon and the drawing mechanism being activatable to move the tip ejector relative to the tip receiving portion between a withdrawn position and an ejection position, the tip ejector being positioned to eject a pipette tip from the tip receiving portion when the tip ejector is moved to the ejection position.

9. The sensor assembly of claim 8 wherein the sensor carrier has a probe cover attached to the receiving member, the probe cover defining an interior area sized to contain the sensing area of the probe, the receiving member being movable relative to the probe cover between a sensor exposed position and a sensor retracted position, the tip ejector being in engagement with the drawing mechanism when the probe cover is in the sensor-retracted position for ejection of the pipette tip and the tip ejector being out of engagement with the drawing mechanism when the probe cover is in the sensor-extended position to prevent ejection of the pipette tip.

10. The sensor assembly of claims 1, 2, 3, 4, or 5 further comprising a probe cover attached to the receiving member, the probe cover defining an interior area sized to contain the sensing area of the probe, the receiving member being movable with the sensor as a unit relative to the probe cover for movement of the probe between a first position with the sensing area of the probe contained in the interior area of the probe cover and a second position with the sensing area of the probe being exposed and exterior of the interior area.

11. The sensor assembly of claim 10 wherein the sensor carrier includes detents that releasably retain the probe cover in the first and second positions.

12. The sensor assembly of claim 10 wherein the receiving member is slidably connected to the probe cover for movement of the probe between the first and second positions.

13. The sensor assembly of claim 10 wherein the probe cover is a generally cylindrical tube.

14. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is removably connected to the receiving member.

15. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is a fiber optic sensor and the probe is a fiber optic probe.

16. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor has a connecting member attached to the probe, and the receiving member is attachable to the connecting member of the sensor.

17. The sensor assembly of claim 1, 2, 3, 4, or 5, further including a protective storage housing removably attachable to the sensor, the protective storage housing extending over at least a portion of the probe and containing the sensing area.

18. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor is a surface plasmon resonance sensor.

19. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the receiving member is removably attachable to the signal carrying member.

20. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the receiving member is integrally connected to the signal carrying member.

21. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensor includes a connecting member connected to the probe, and the receiving member is attached to the connecting member.

22. The sensor assembly of claim 1, 2, 3, 4, or 5 wherein the sensing area is between the first end portion and the second alignment end portion.

23. The sensor assembly of claim 3 ,4, or 5, further comprising a pipette tip removably connected to the pipette and positioned to receive the sensing area of the sensor therein, the pipette tip including a lower tip portion having a first cross-sectional area, an upper tip portion having a second cross-sectional area, and a constricted middle portion between the lower and upper tip portions, the constricted middle tip portion having a third cross-sectional area that is less than the first and second cross-sectional areas of the lower and upper tip portions.

24. The sensor assembly of claim 3, 4, or 5, further comprising a pipette tip connected to the pipette and positioned to receive the sensing area of the sensor therein, the pipette tip having a first tip portion and a second tip portion removably attached to the first portion, the first tip portion being adapted to retain sample volumes ranging from 2 to 20 microliters, inclusive.

25. The sensor assembly of claim 3, 4, or 5, further comprising a pipette tip connected to the pipette and positioned to receive the sensing area of the sensor therein, the

sensing area being movable laterally relative to the pipette tip when the sensing area is in the pipette tip, the pipette tip being adapted to allow the sensing area of the wave guide probe to waggle between a first extended position and a second axial position when the volume of a selected sample within the pipette is oscillated.

26. The sensor assembly of claim 25 wherein the pipette has first and second shoulder portions axially and laterally offset from each other to define a laterally offset interior area.

27. The sensor assembly of claim 26 wherein the interior area has a substantially Z-shaped cross-sectional area.

28. The sensor assembly of claim 3, 4, or 5 wherein the pipette has a retaining portion that engages the wave-guide-sensor carrier and releasably retains the wave guide receiving member.

29. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is a sample (bulk) solution absorbance sensor.

30. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is an electrochemical sensor and the probe is an electronic probe.

31. The sensor assembly of claims 1, 2, 3, 4, or 5, wherein the sensor is a surface acoustic wave sensor, and the probe is an electronic probe.

32. A method of analytically sampling a selected chemical sample with a sensor assembly coupled to an analyzer and a signal source, comprising the steps of:

providing a sensor carrier with a receiving member coupled to the analyzer and the signal source by a signal carrying member, the receiving member having a coupler and a sensor cover attached to the coupler;

removably attaching the sensor to the receiving member and connecting an end portion of the sensor with the signal carrying member, the sensor having a sensing area spaced apart from the end portion of the sensor;

propagating a selected signal between the signal source and the sensing area of the sensor through the signal carrying member and the sensor;

moving the sensor relative to the sensor cover from a sensor contained position with the sensing area of the sensor being covered by the sensor cover to a sensor extended position with the sensing area being exterior of the sensor cover and exposed;

contacting the selected chemical sample with the sensing area of the sensor after the sensor is attached to the receiving member and the sensor is in the sensor extended position; and

analyzing with the analyzer the signal thereto through the signal carrying member from the sensing area of the sensor when the sensing area is contacting the selected chemical sample to analytically sample the selected chemical sample.

33. The method of claim 32, further including the steps of withdrawing the sensor from the selected chemical sample and moving the sensor from the sensor extended position to the sensor contained position with the sensing area being covered by the sensor cover.

34. The method of claim 33, further including the steps of moving the sensor to the sensor extended position after the sensor has been withdrawn to the sensor contained position, and then contacting the sensing area with a second selected chemical sample when the sensor is in the sensor extended position.

35. The method of claim 34 wherein the sensor is a first sensor, and further including the steps of removing the first sensor from the receiving member after chemically analyzing the selected chemical sample, and removably attaching a second sensor to the sensor carrier.

36. The method of claim 32 wherein the step of contacting the selected chemical sample with the sensing area of the sensor includes moving the selected chemical sample into contact with the sensing area, and the step of analyzing with the analyzer occurs substantially simultaneously as the selected chemical sample is moved into contact with the sensing area of the sensor.

37. The method of claim 32, further including the step of oscillating the sample relative to the sensor when the sensing area of the sensor is in contact with the selected chemical sample.

38. The method of claim 32 or 37, further including the step of moving the sensor laterally relative to the sample when the sensing area of the sensor is in contact with the selected chemical sample.

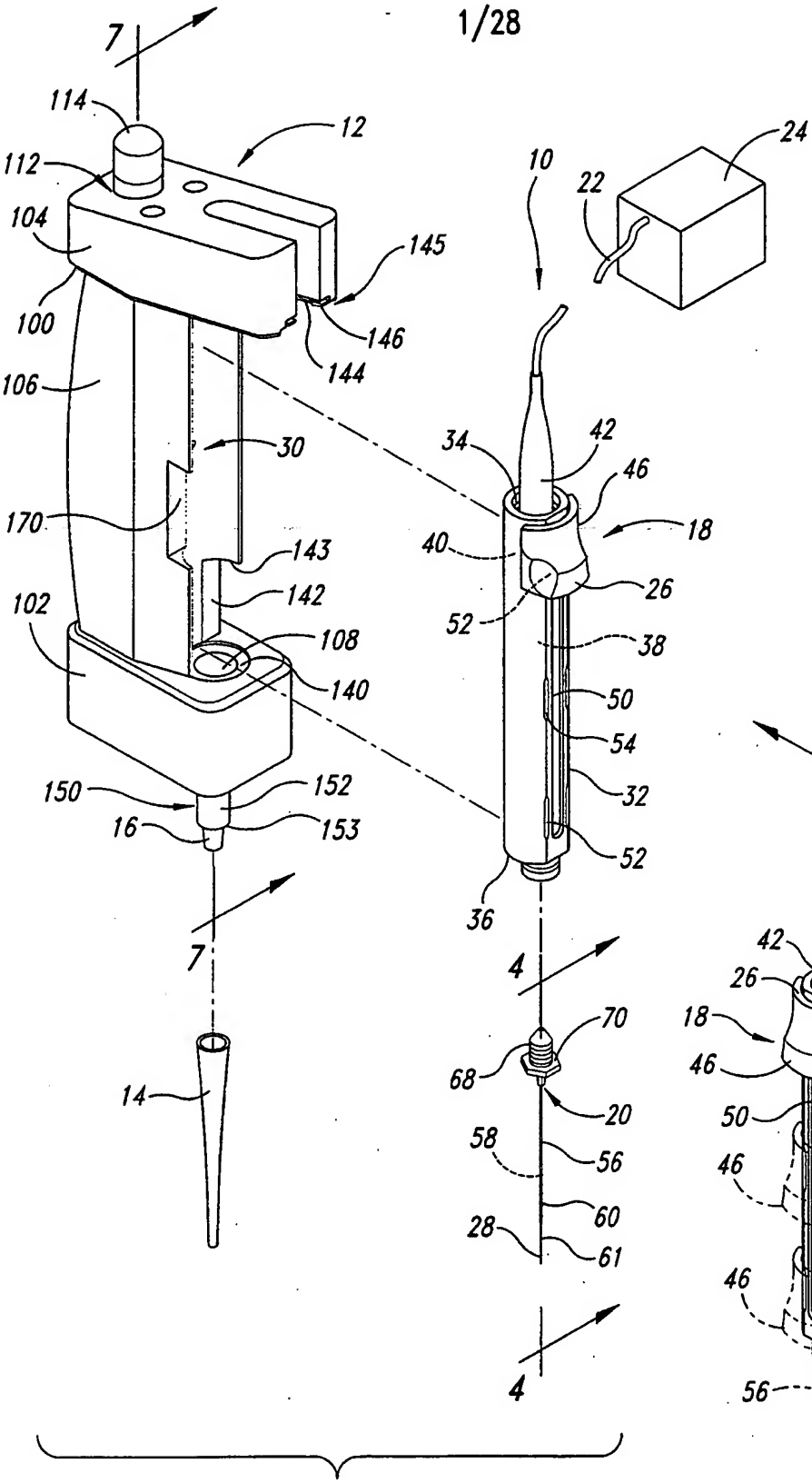
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Fig. 1

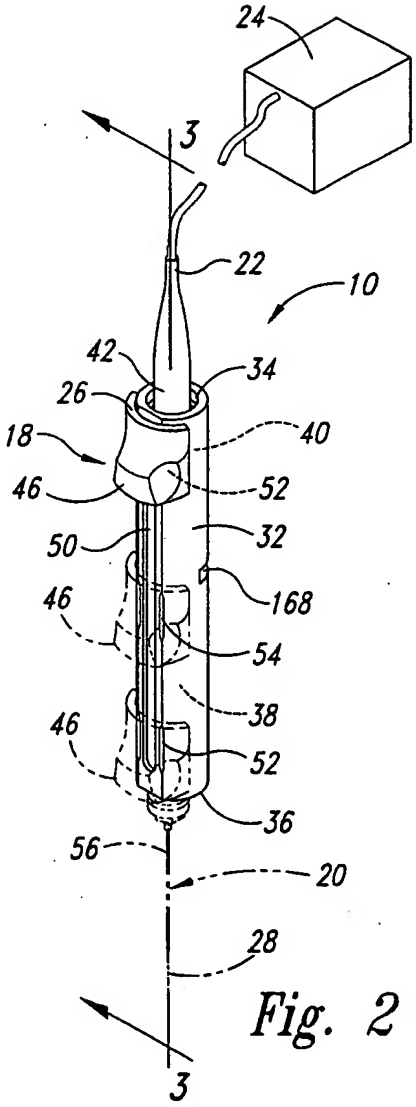
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Fig. 2

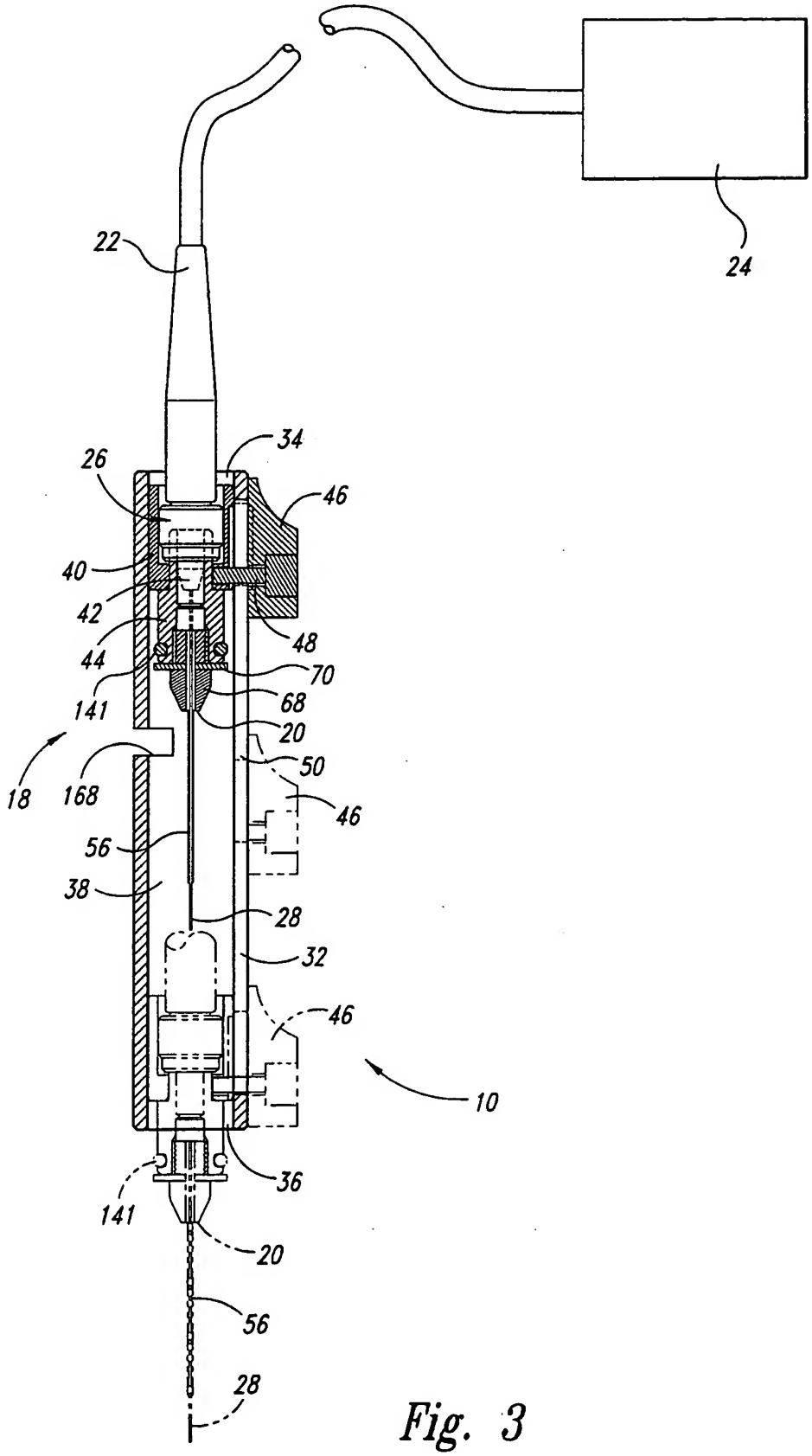
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Fig. 3

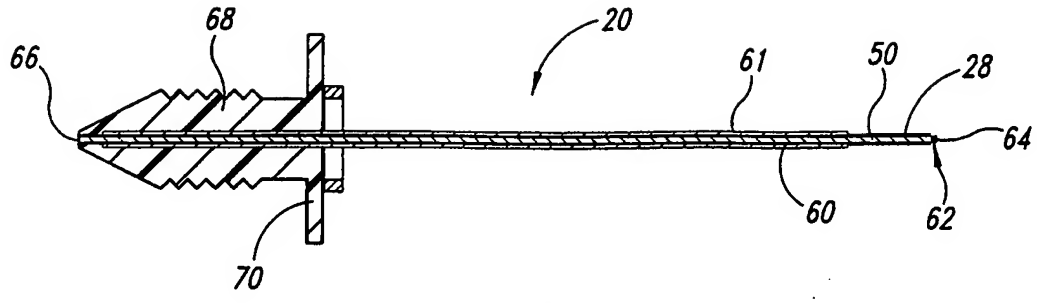


Fig. 4

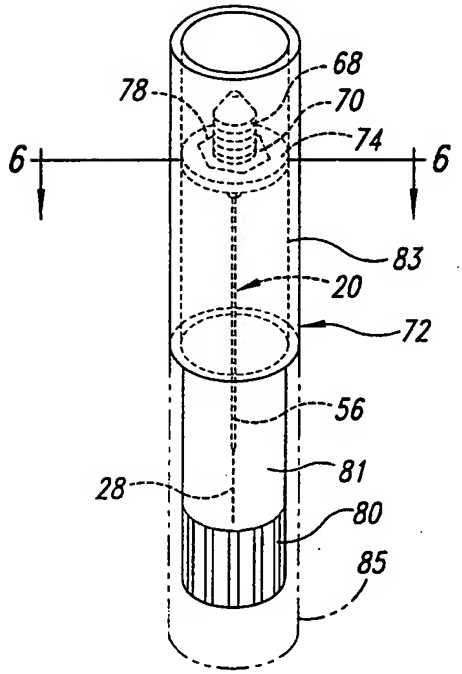
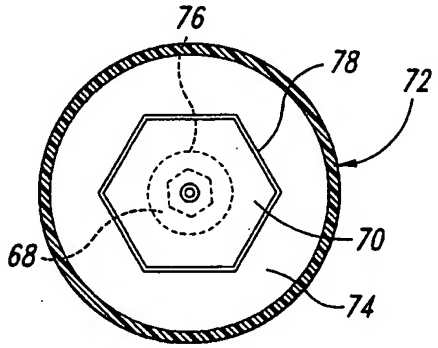


Fig. 5



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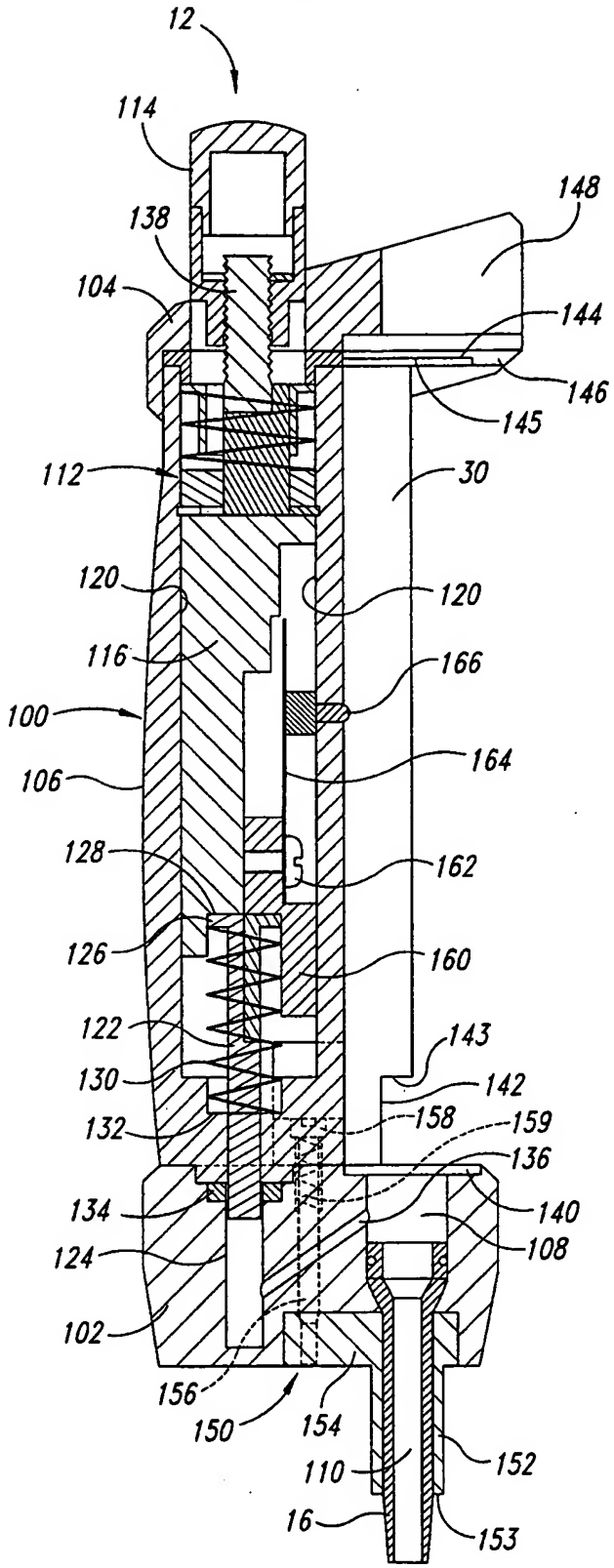
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Fig. 7

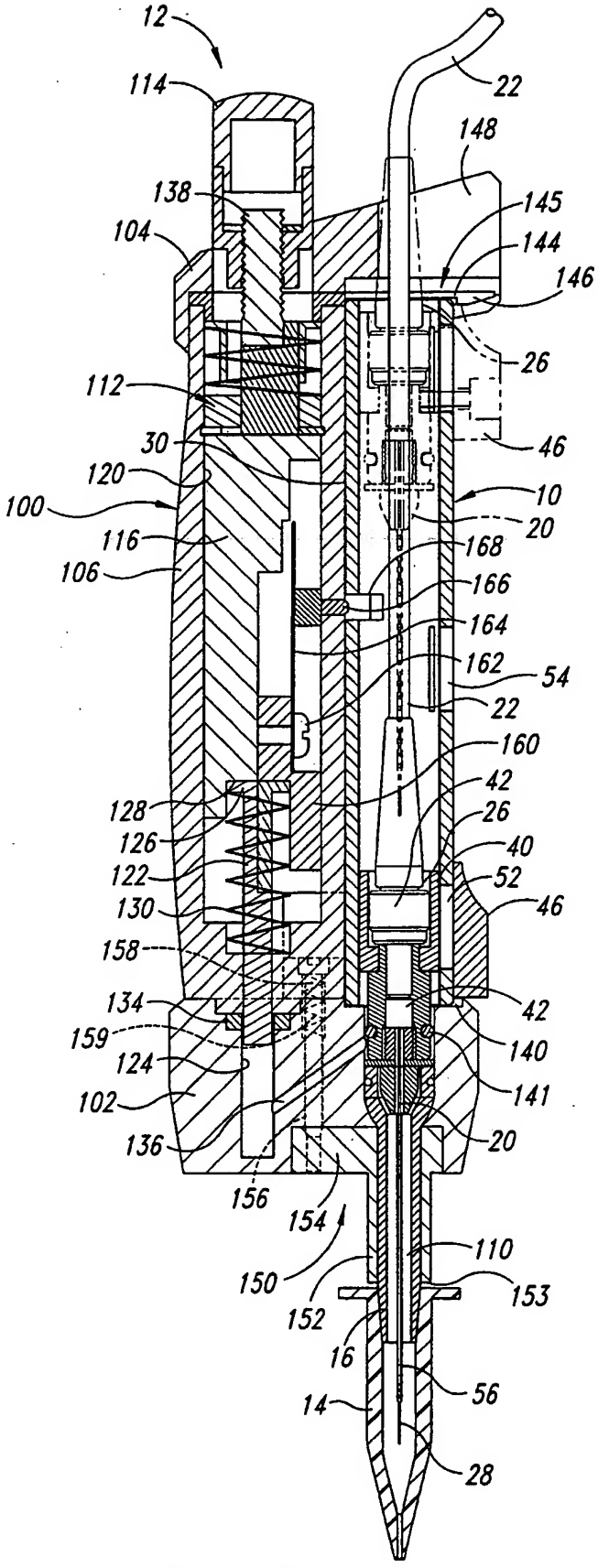
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Fig. 8

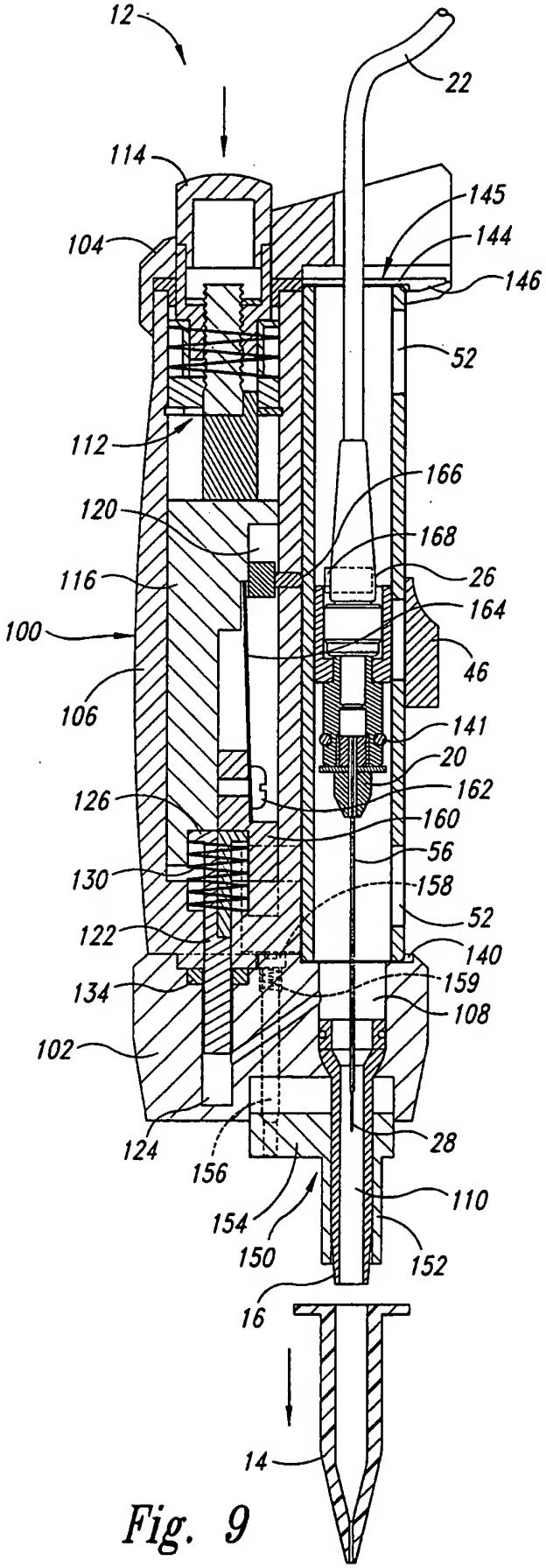
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Fig. 9

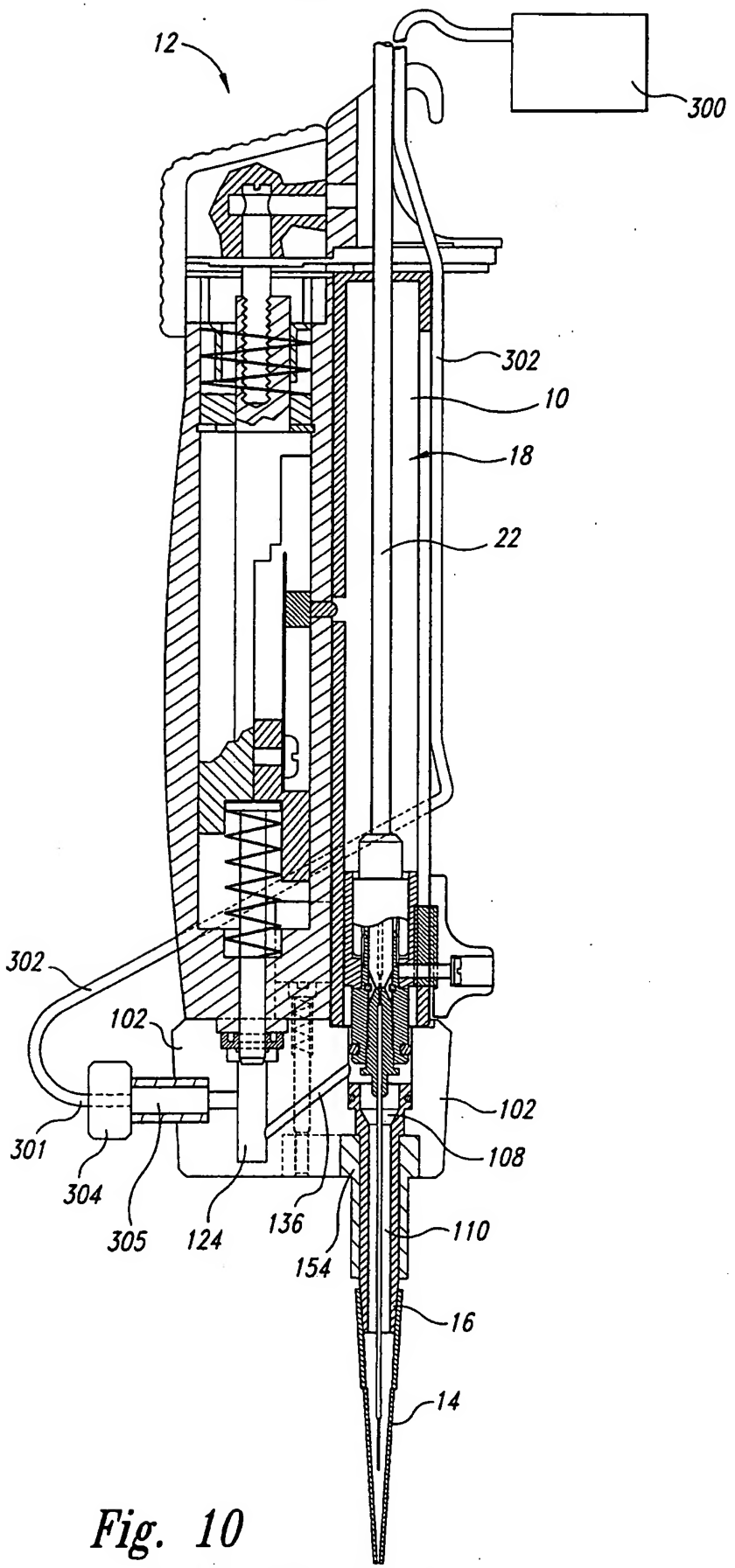
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Fig. 10

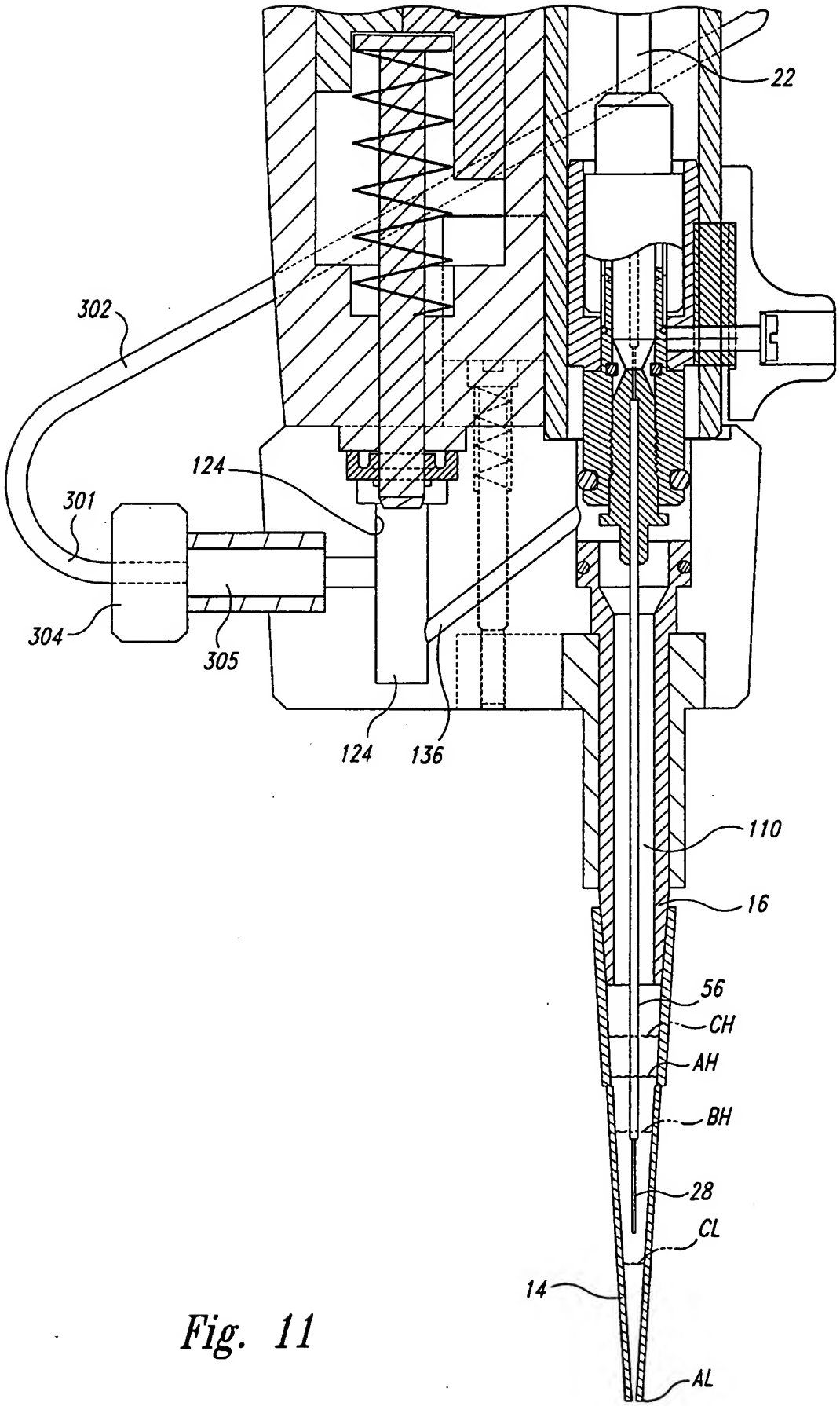
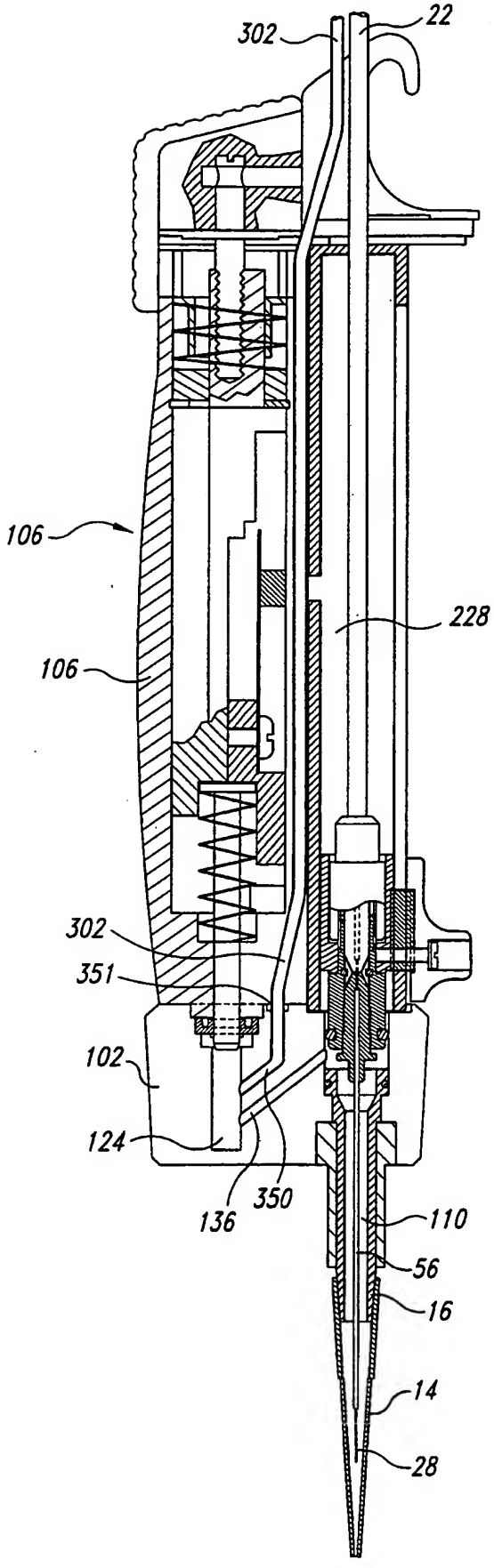


Fig. 11



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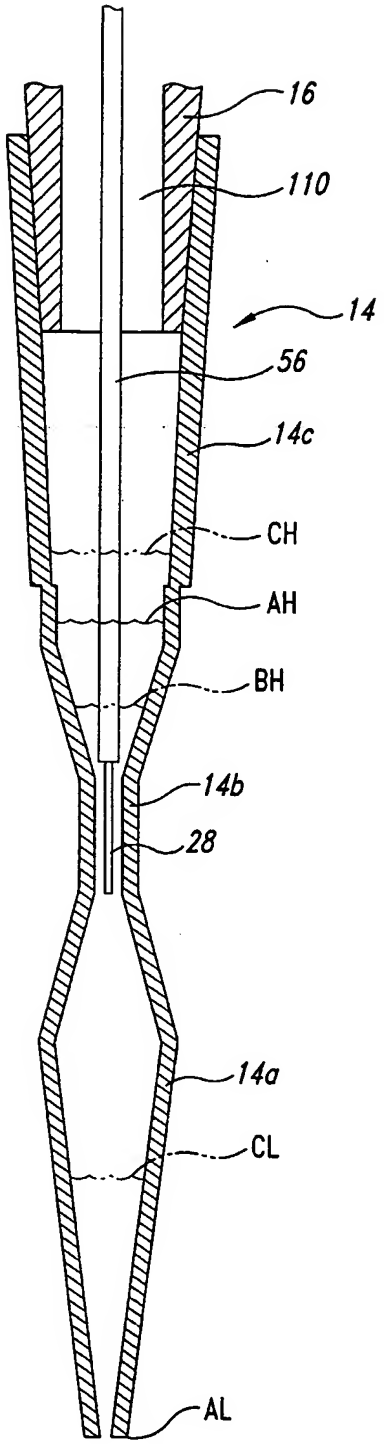
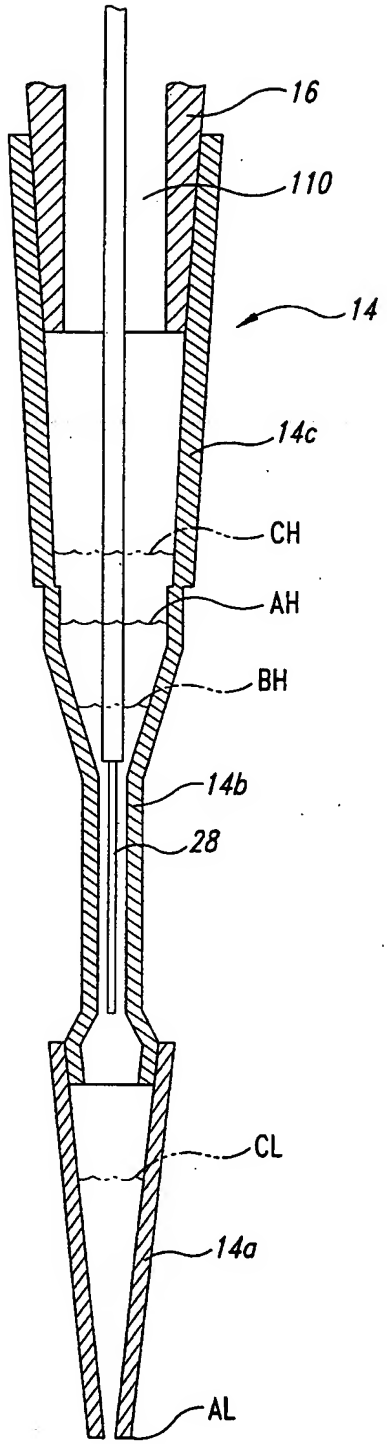


Fig. 13



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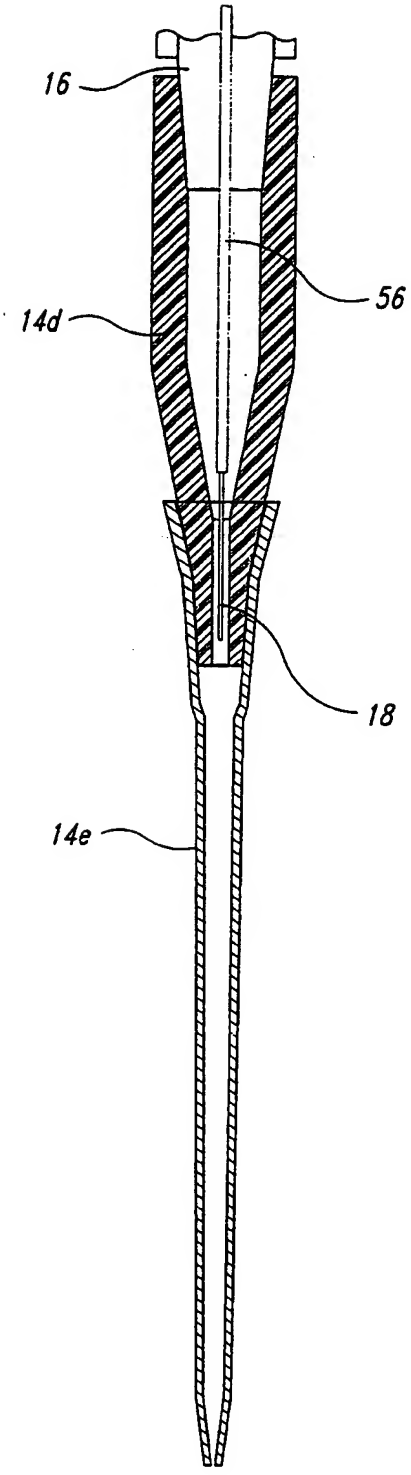

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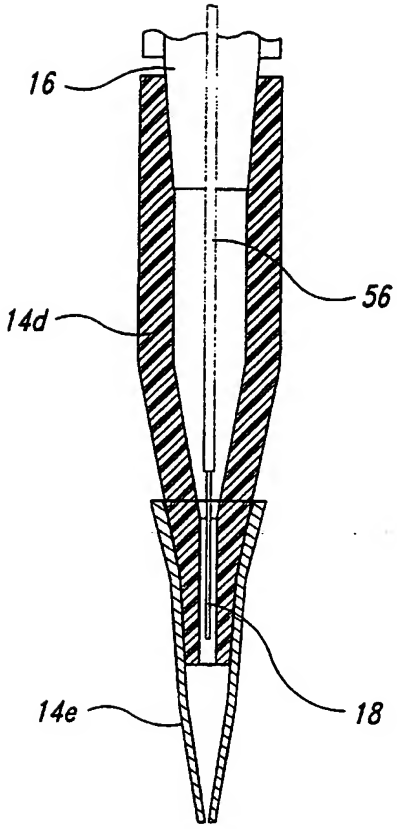

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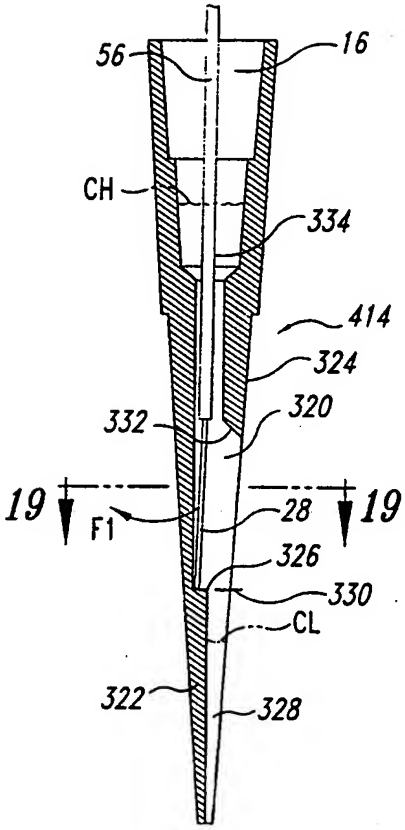
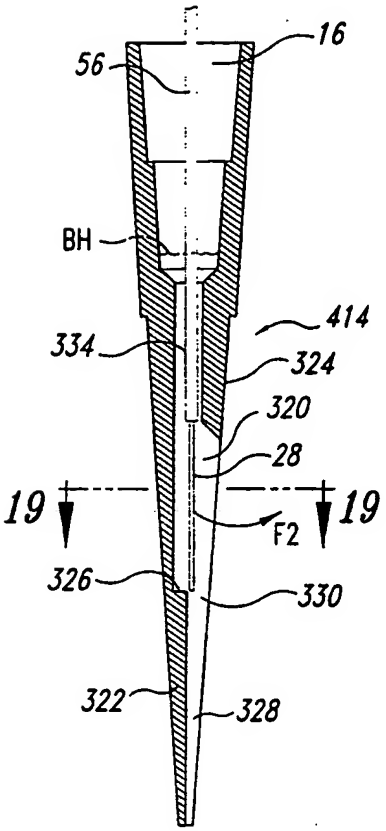


Fig. 17



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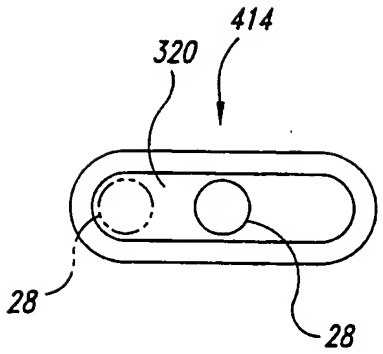

Fig. 19

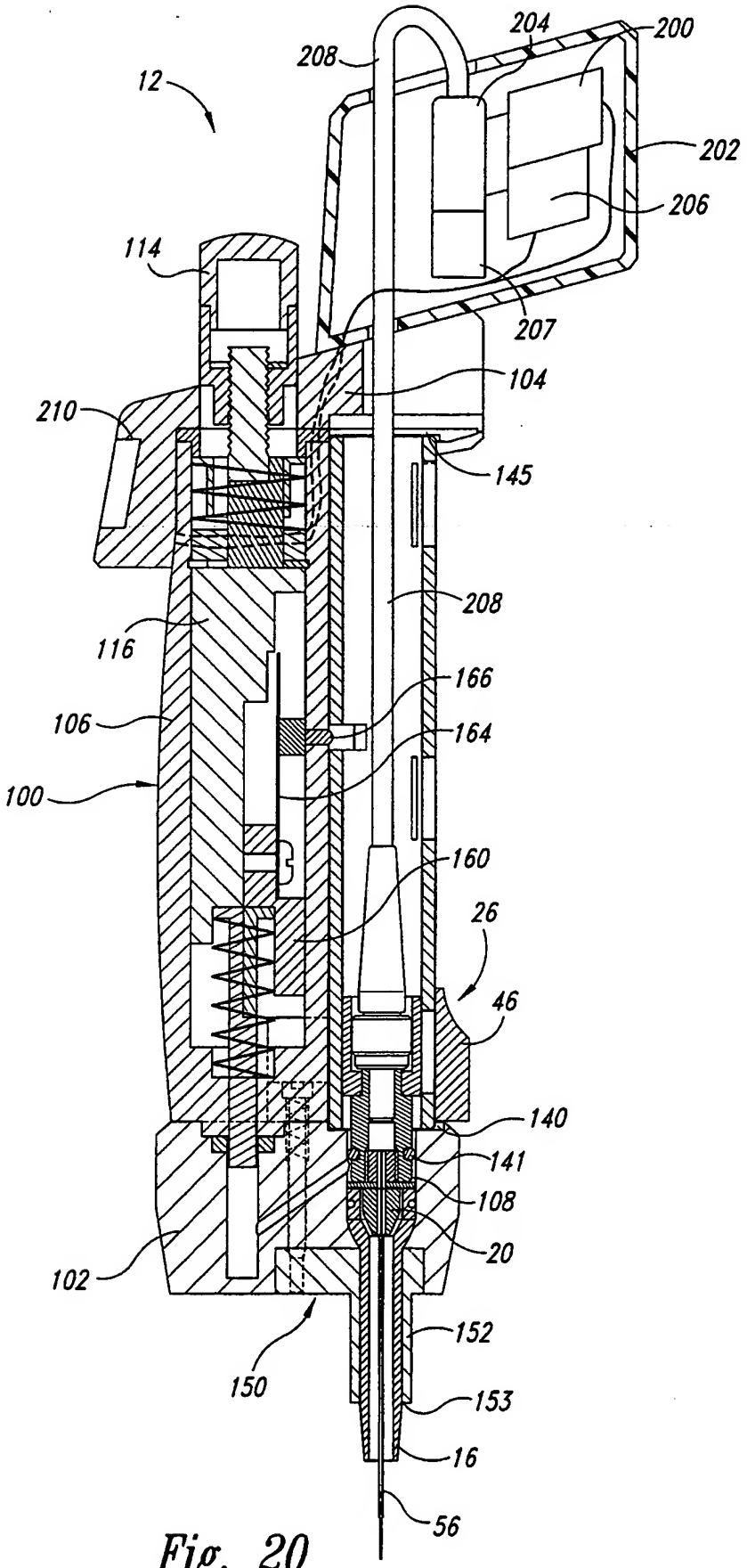
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Fig. 20

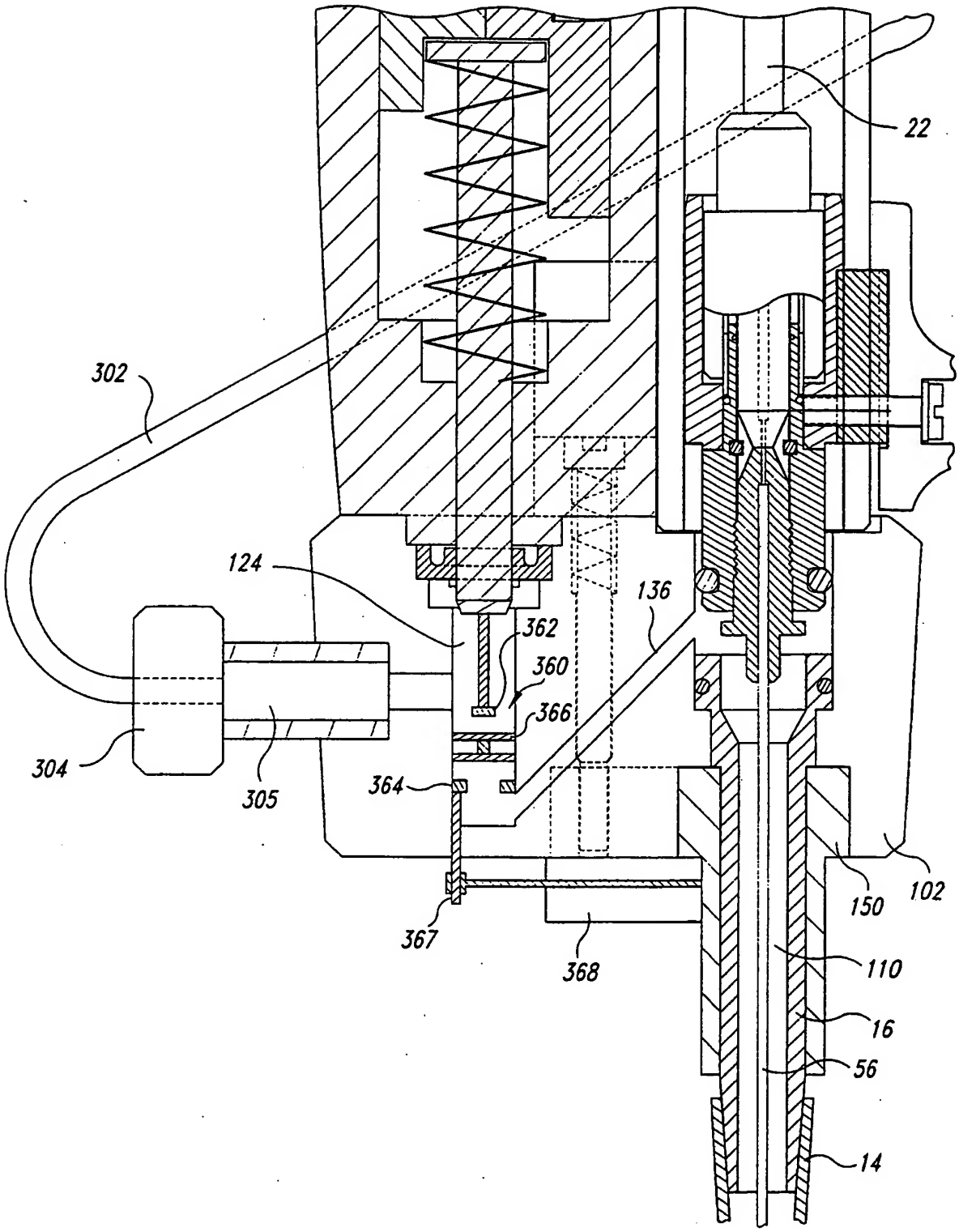
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Fig. 21

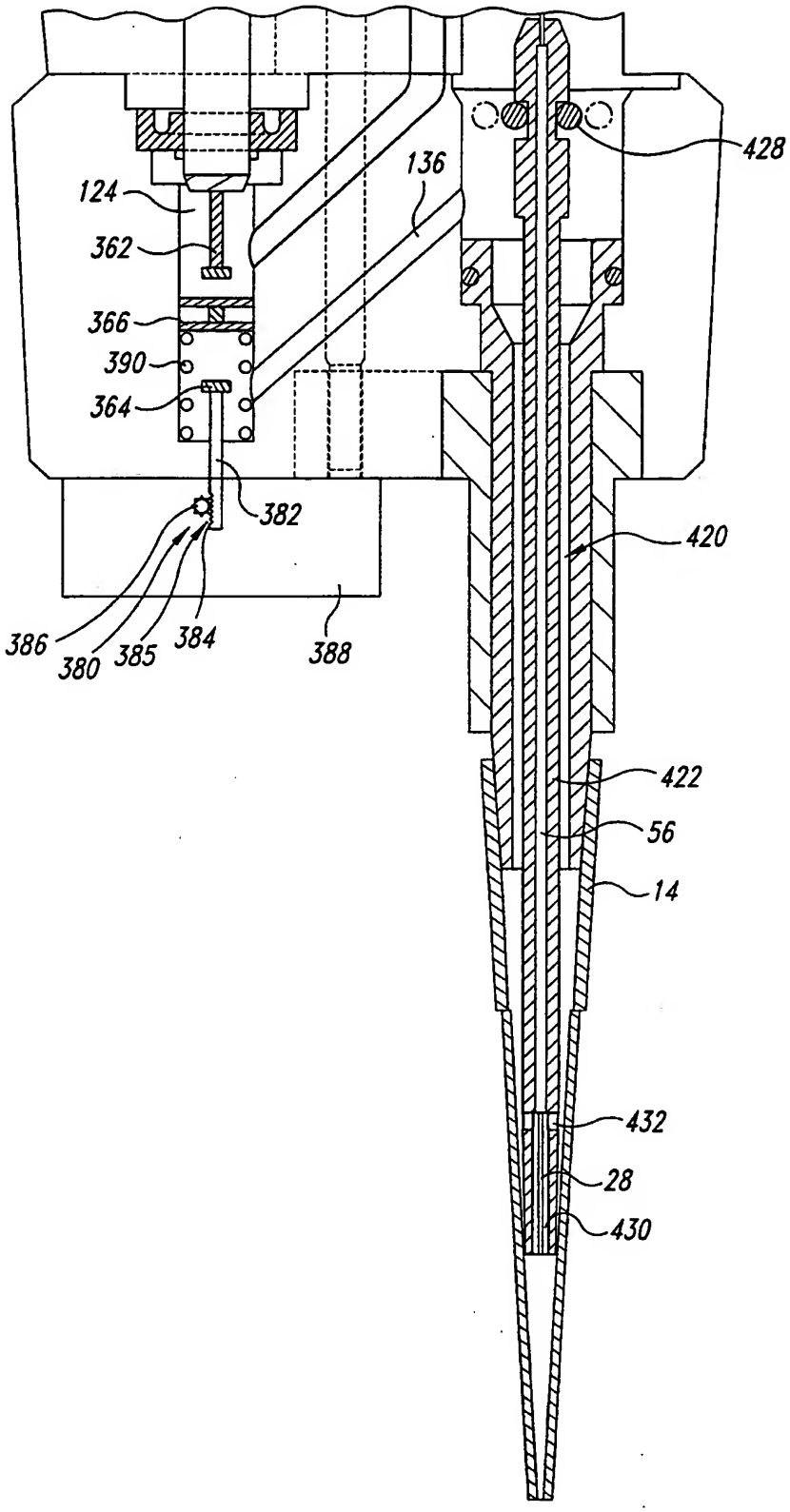
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Fig. 22

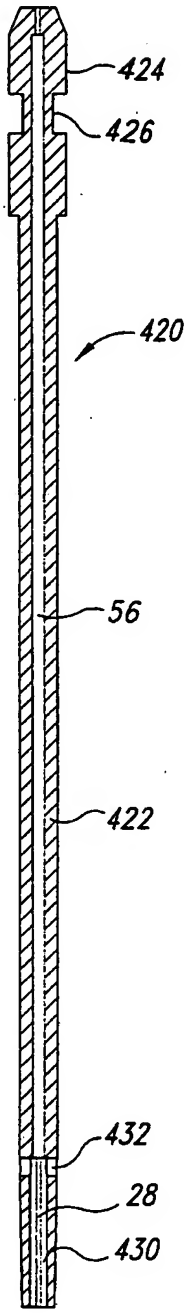
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Fig. 24

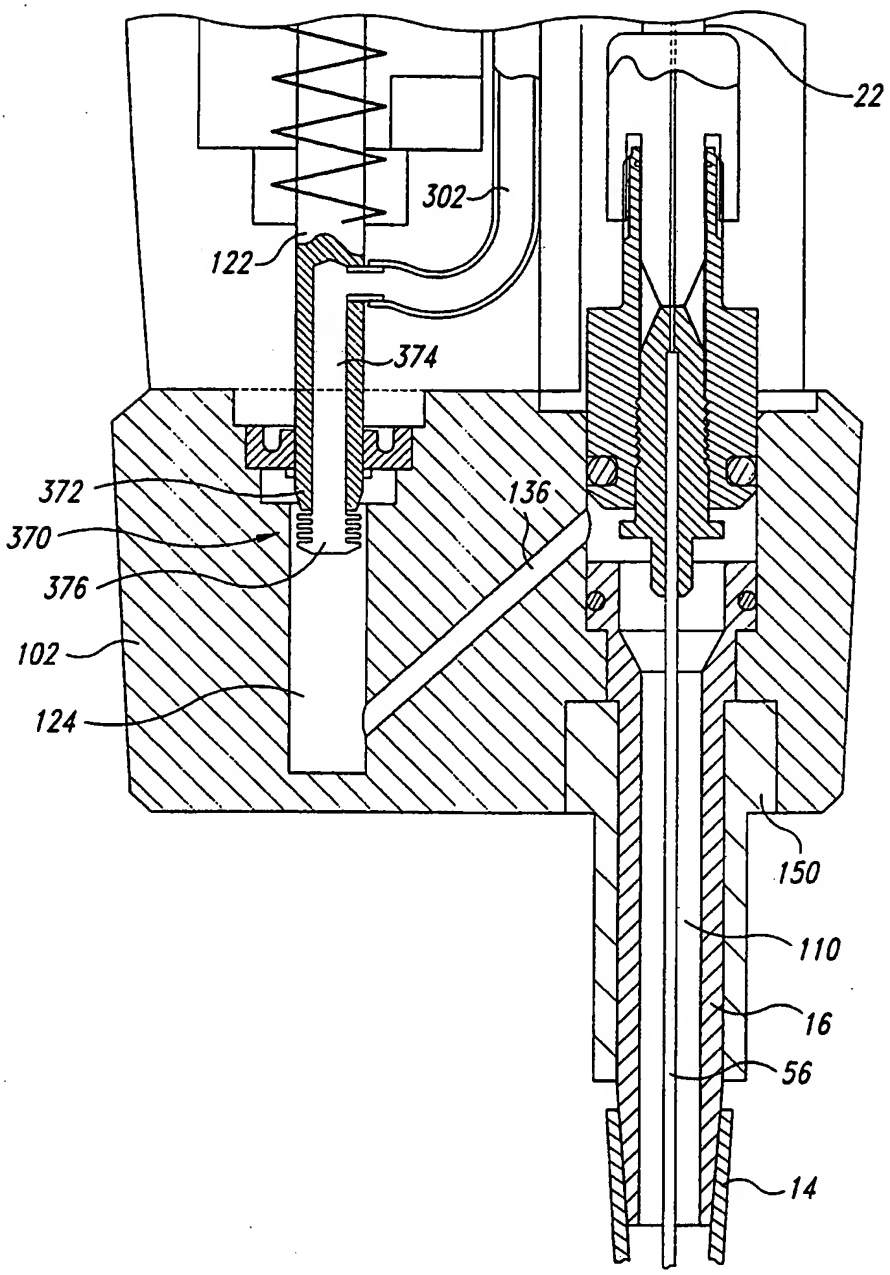
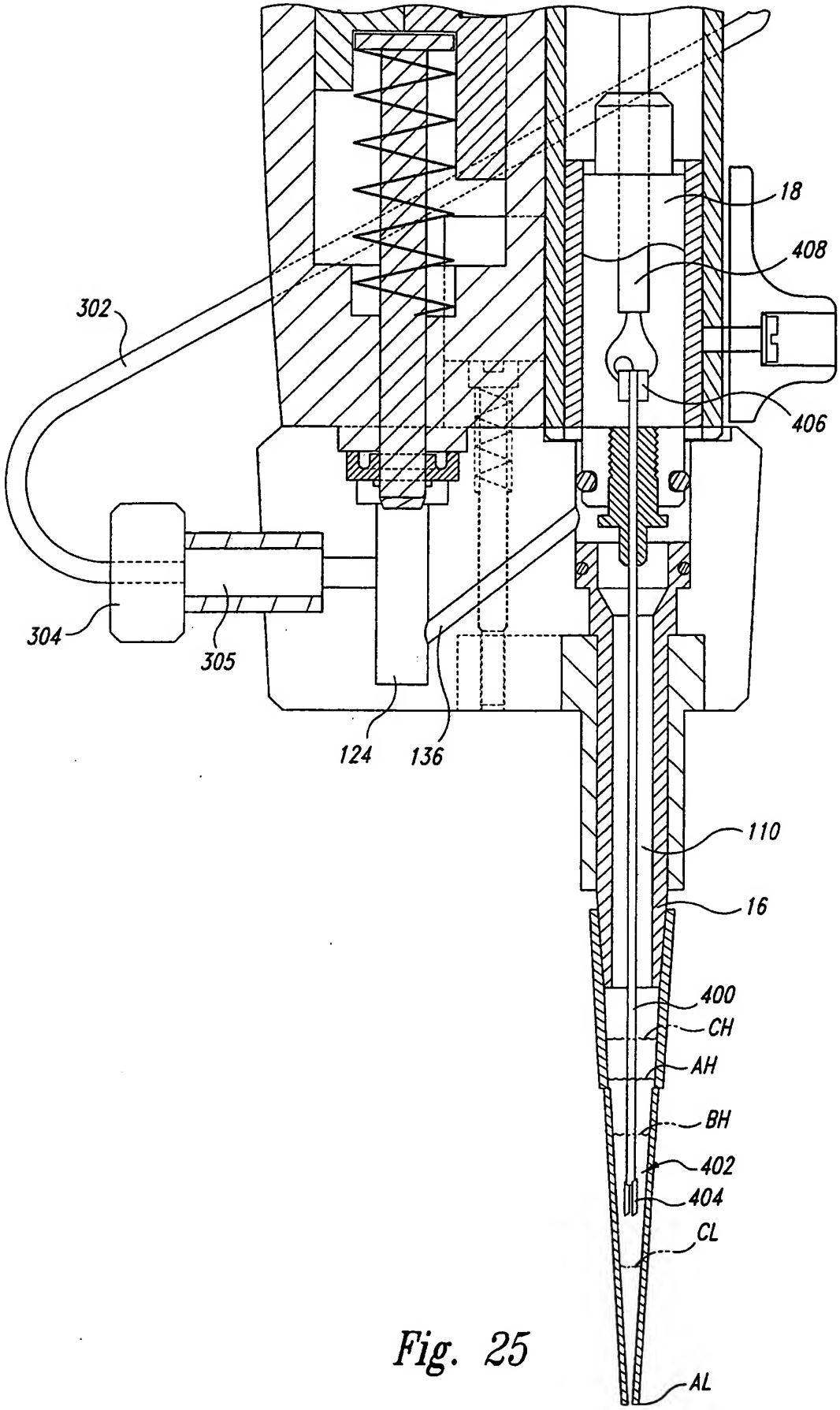


Fig. 23



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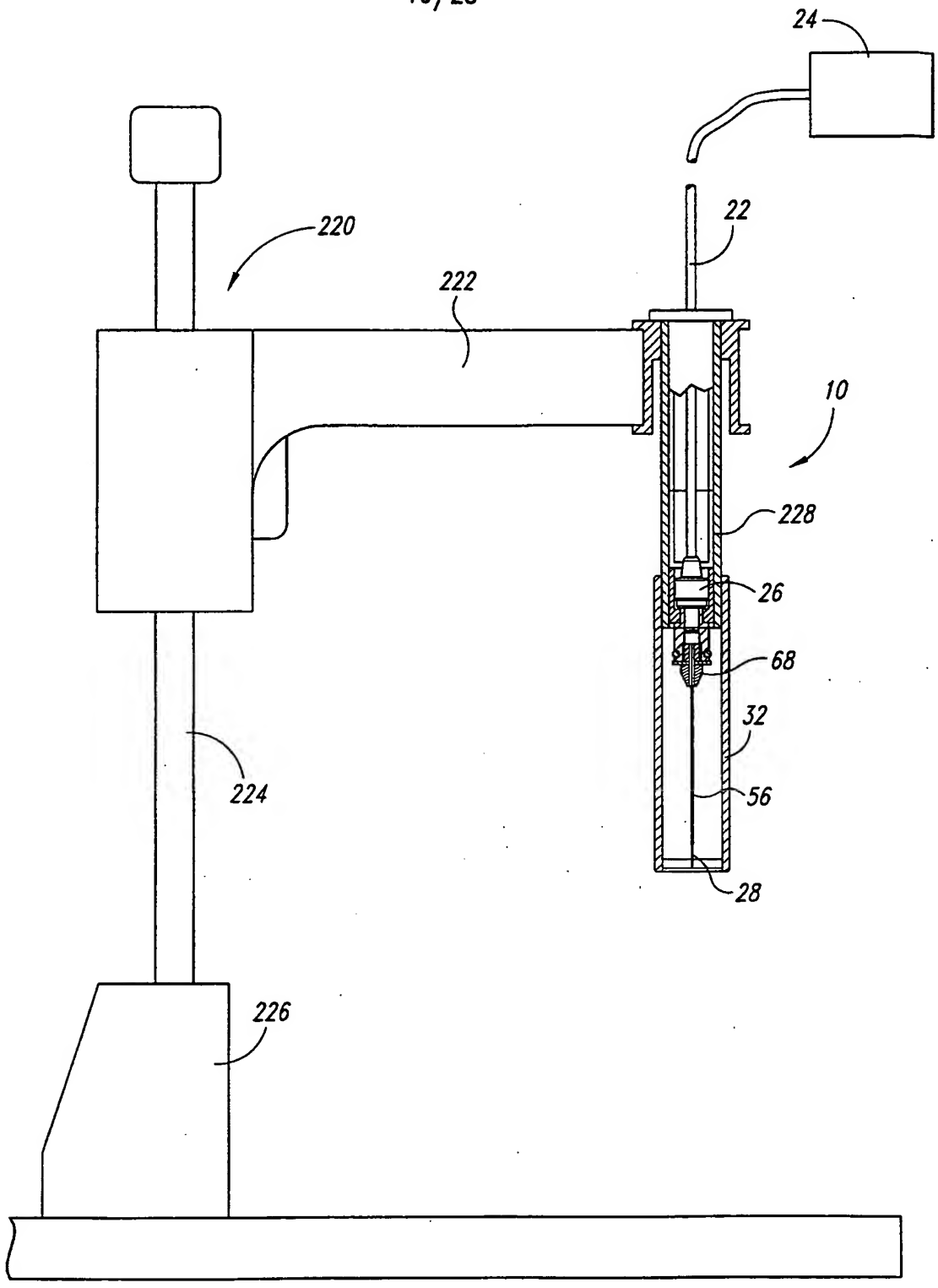
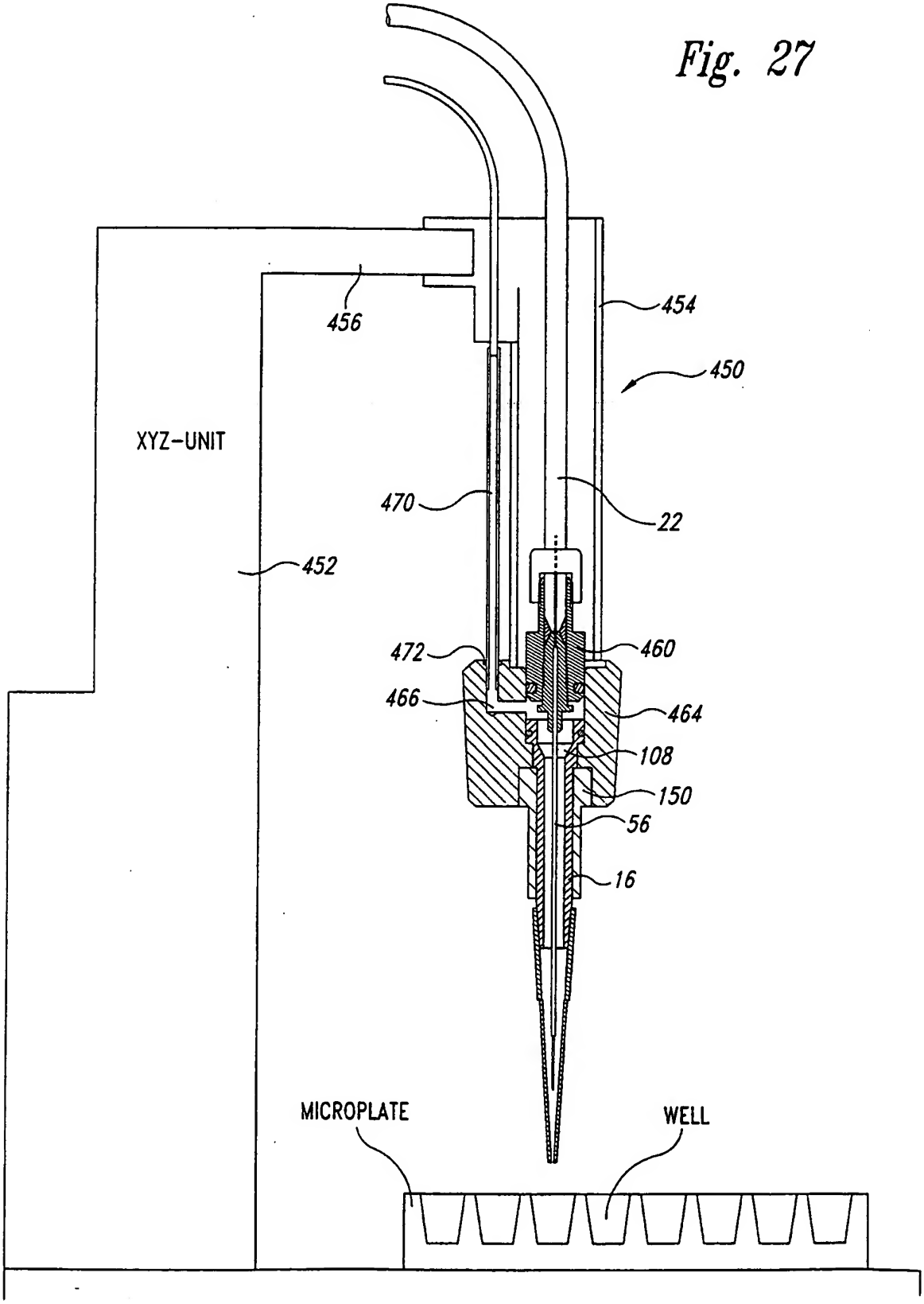


Fig. 26

Fig. 27


456
454
450
XYZ-UNIT
470
22
452
472
460
466
464
108
150
56
16
MICROPLATE
WELL

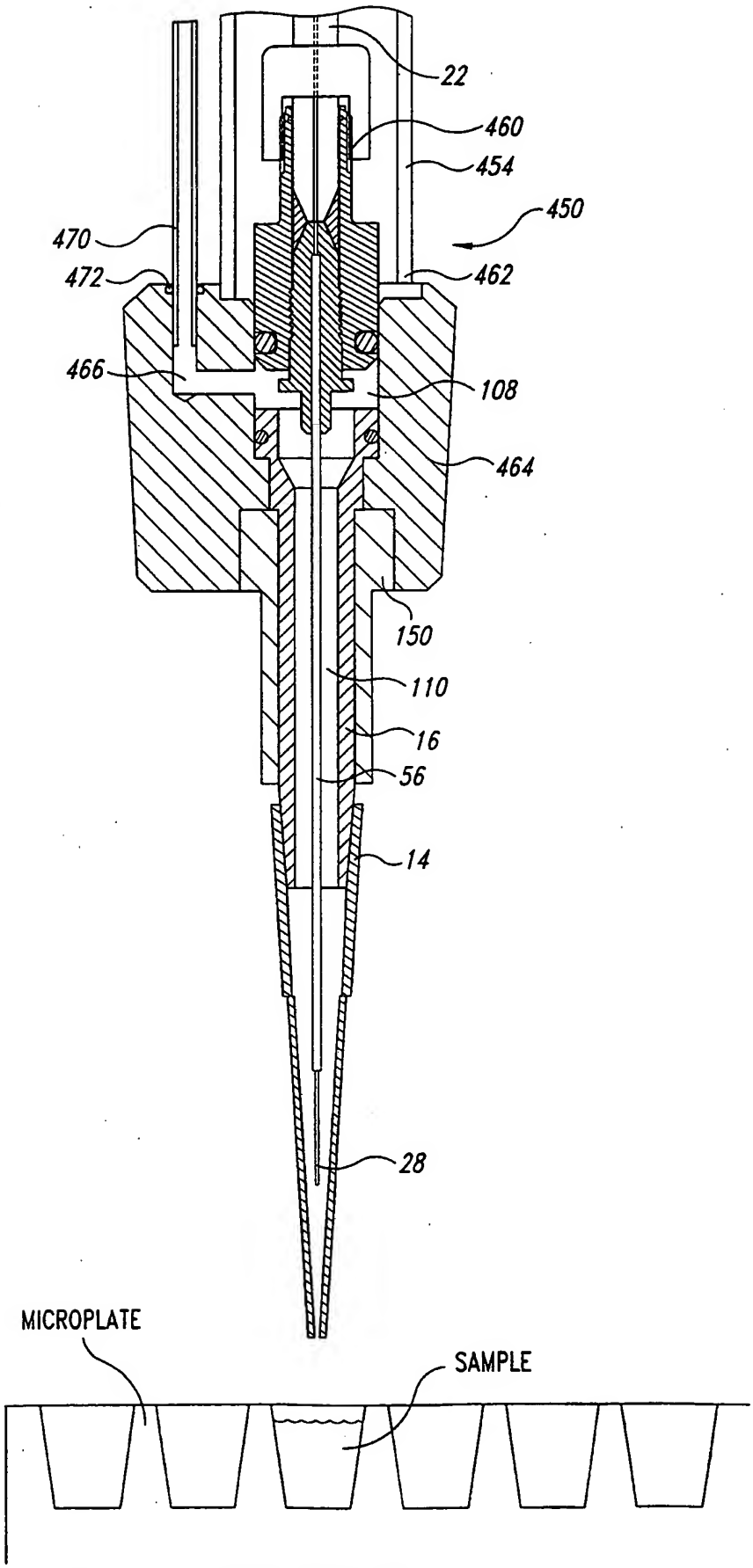

22
460
454
450
470
472
462
466
108
464
150
110
16
56
14
28
MICROPLATE
SAMPLE

Fig. 28

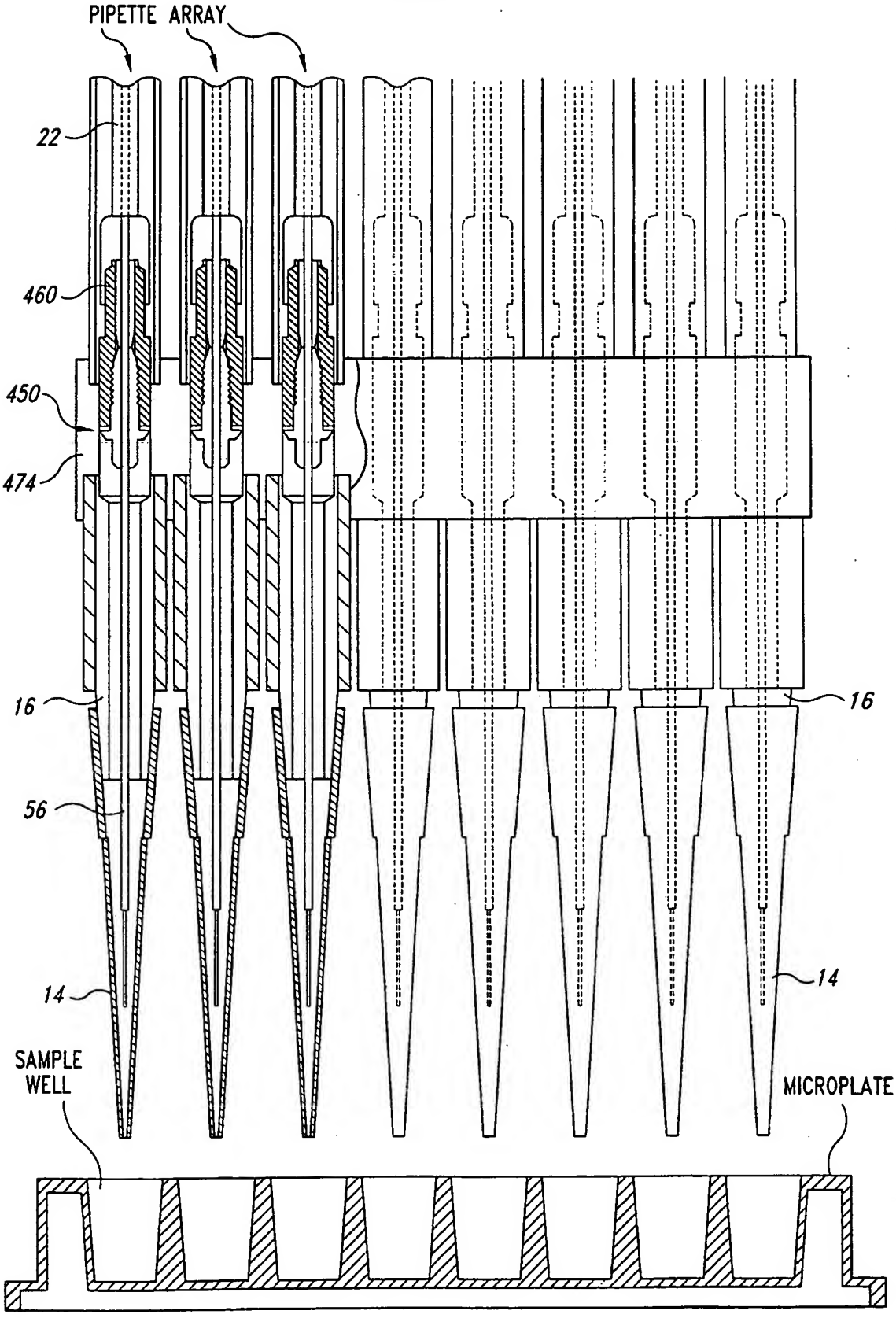

PIPETTE ARRAY
22
460
450
474
16
16
56
14
14
SAMPLE WELL
MICROPLATE

Fig. 29

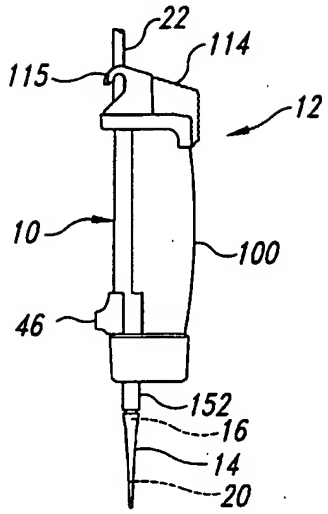


Fig. 30A

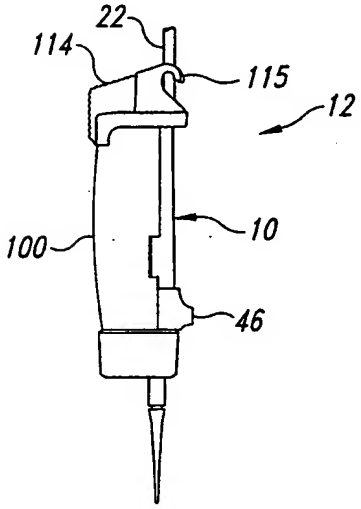


Fig. 30B

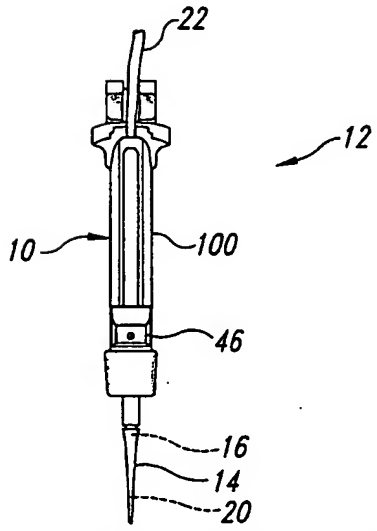


Fig. 30C

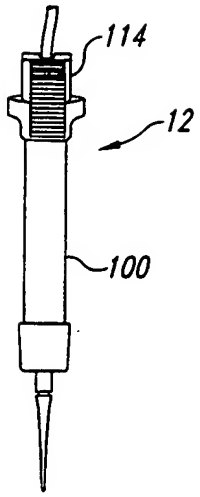


Fig. 30D

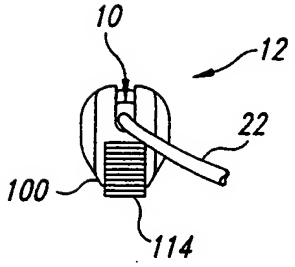


Fig. 30E

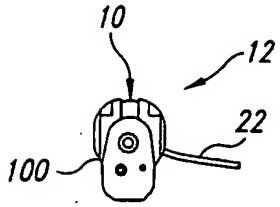


Fig. 30F

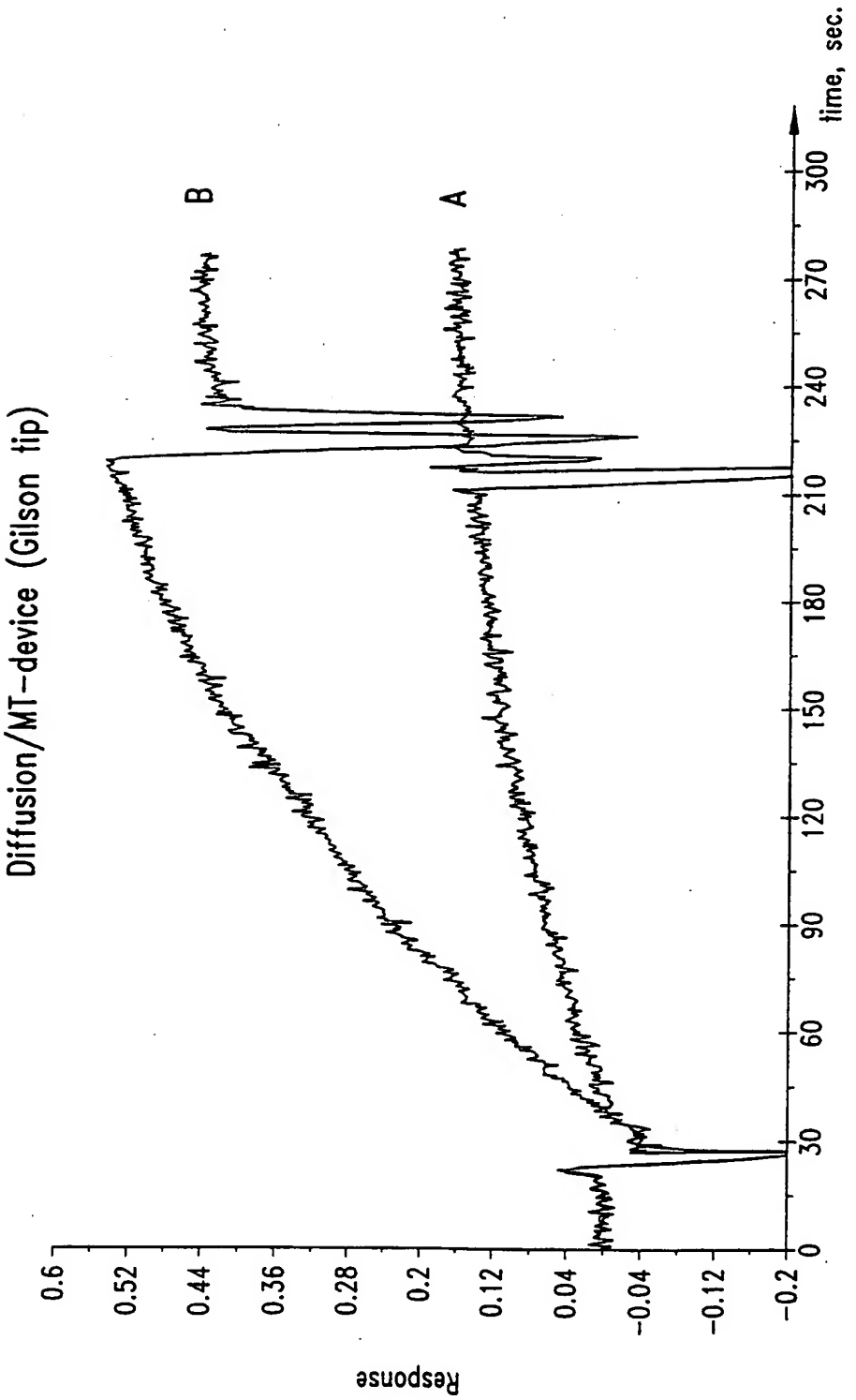

Diffusion/MT-device (Gilson tip)
B
A
time, sec.
Response
0.6
0.52
0.44
0.36
0.28
0.2
0.12
0.04
-0.04
-0.12
-0.2
0
30
60
90
120
150
180
210
240
270
300

Fig. 31

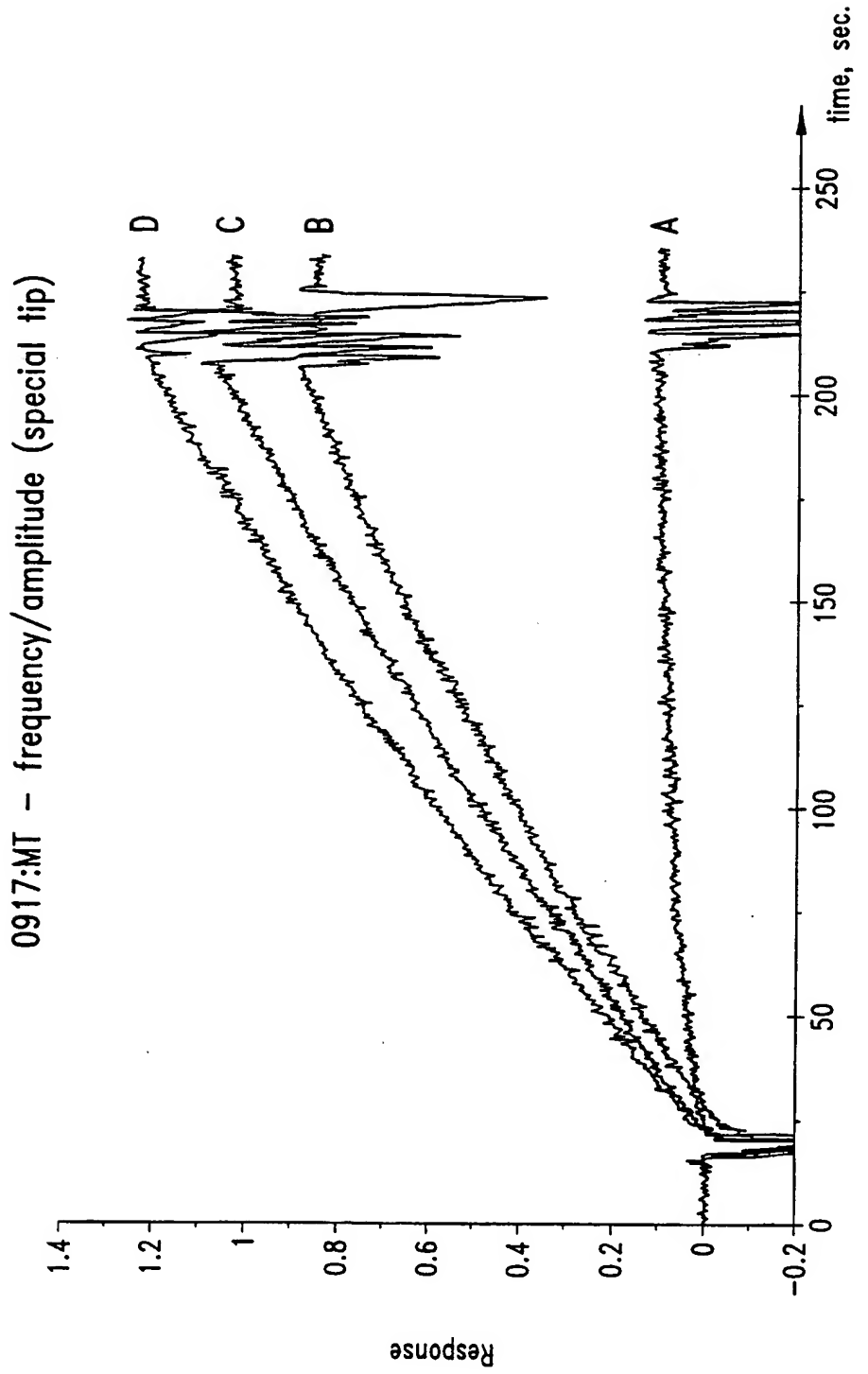

0917:MT - frequency/amplitude (special tip)
D
C
B
A
time, sec.
0
50
100
150
200
250
-0.2
0
0.2
0.4
0.6
0.8
1
1.2
1.4
Response

Fig. 32A

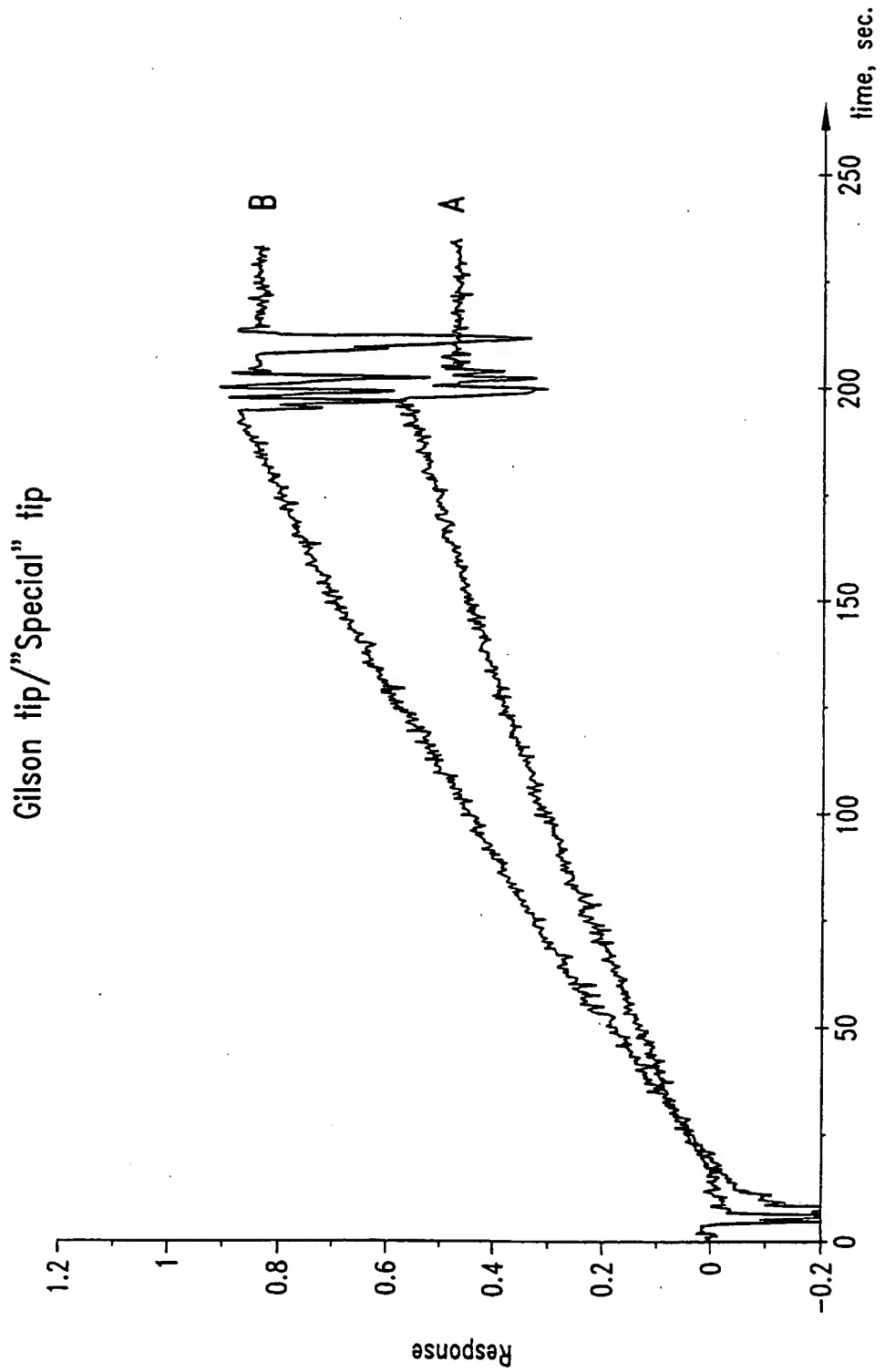

Gilson tip/"Special" tip
B
A
time, sec.
Response
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0
50
100
150
200
250

Fig. 32B

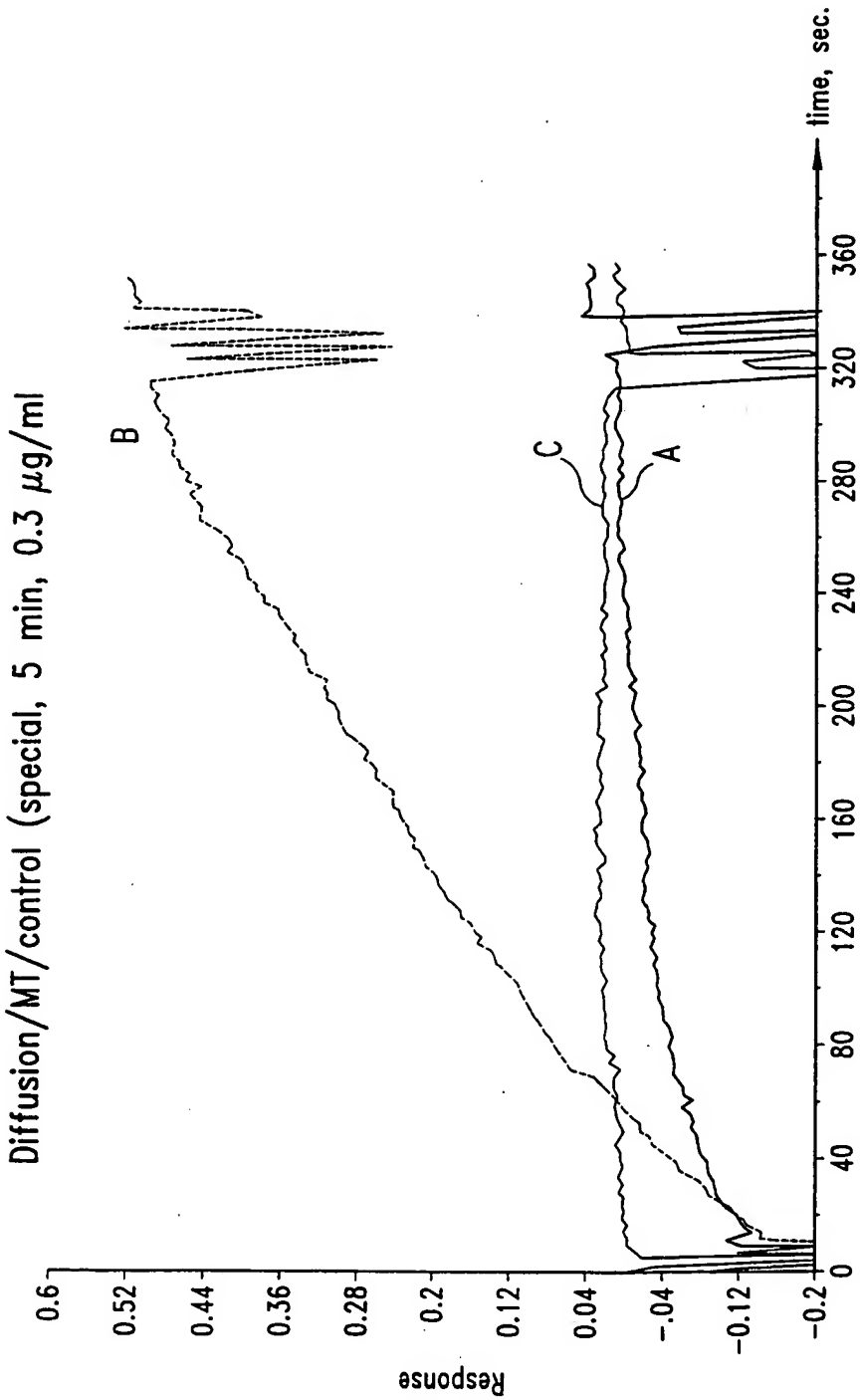

Diffusion/MT/control (special, 5 min, 0.3 μg/ml
B
C
A
time, sec.
0
40
80
120
160
200
240
280
320
360
Response
0.6
0.52
0.44
0.36
0.28
0.2
0.12
0.04
-.04
-0.12
-0.2

Fig. 32C

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/US 98/01370

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N21/03 B01L3/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G01N B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 076 406 A (MILES LAB) 13 April 1983 see page 6, line 19 - page 8, line 25 see claims 1,6,7; figure 2	1-3,15
Y		4,18
A		32

Y	WO 96 37302 A (RAININ INSTR CO INC) 28 November 1996 see claim 1	4
A		6

Y	US 5 359 681 A (JORGENSON RALPH C ET AL) 25 October 1994 cited in the application see claim 1	18
A		1,2

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 May 1998	04/06/1998

Name and mailing address of the ISA	Authorized officer
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2

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 98/01370

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 87 06008 A (BECKMAN INSTRUMENTS INC) 8 October 1987 see page 27, paragraph 2 - page 29, paragraph 1 see page 39, paragraph 3 - page 40, paragraph 3	1,2,15
A	US 4 240 751 A (LINNECKE CARL B ET AL) 23 December 1980 see column 16, line 37 - column 17, line 40 see figures 1,9	1,2,15

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter ional Application No
PCT/US 98/01370

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0076406 A	13-04-1983	US 4488814 A	18-12-1984
		AU 552948 B	26-06-1986
		AU 8707082 A	12-05-1983
		CA 1190408 A	16-07-1985
		CA 1199166 C	14-01-1986
		DE 3278559 A	07-07-1988
		EP 0163826 A	11-12-1985
		JP 58068648 A	23-04-1983
		US 4566203 A	28-01-1986
WO 9637302 A	28-11-1996	US 5614153 A	25-03-1997
		EP 0772493 A	14-05-1997
		JP 10503128 T	24-03-1998
US 5359681 A	25-10-1994	AT 160871 T	15-12-1997
		CA 2153389 A	21-07-1994
		DE 69407161 D	15-01-1998
		DE 69407161 T	26-03-1998
		EP 0678194 A	25-10-1995
		JP 8505475 T	11-06-1996
		WO 9416312 A	21-07-1994
		US 5647030 A	08-07-1997
WO 8706008 A	08-10-1987	EP 0261202 A	30-03-1988
		FI 875113 A	19-11-1987
		JP 8082630 A	26-03-1996
		JP 8054401 A	27-02-1996
		JP 63502931 T	27-10-1988
		US 5104621 A	14-04-1992
		US 5139744 A	18-08-1992
		US 5108703 A	28-04-1992
		US 5125748 A	30-06-1992
		US 5206568 A	27-04-1993
		US 5369566 A	29-11-1994
US 4240751 A	23-12-1980	CA 1122811 A	04-05-1982